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*BAUER, G.E., Med. J. Aust. 2, 911-915 (1970)

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Declinax = Trade Mark

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by Dr. Gabor Kato,
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McGill University, Montreal, Canada

Photographs and drawings by the author

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Photographs by the author

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by Marcel Vertès

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by Gabrielle Wittkop-Ménardeau,
Höhestrasse 29, D-638 Bad Homburg

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Photographs by the author

Gastric Chromography

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Photographs by the author unless otherwise stated

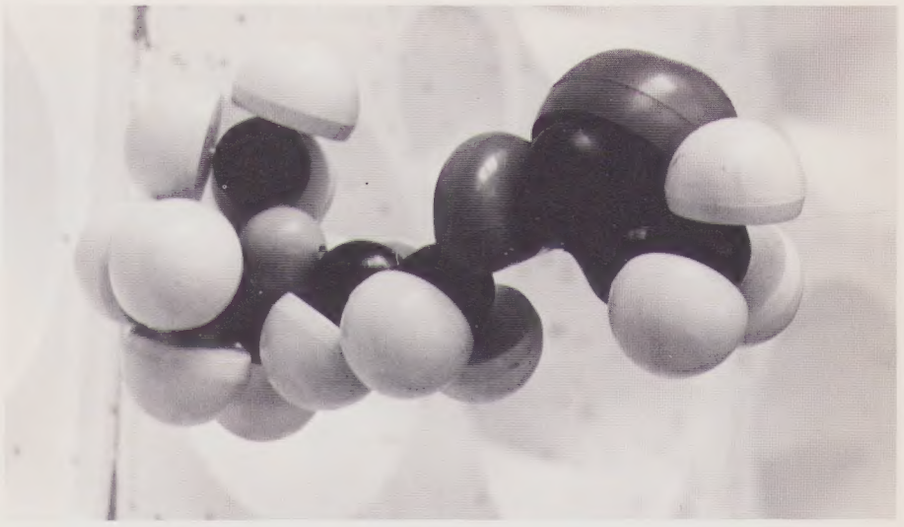
Drug Receptor Research by Nuclear Magnetic Resonance

Gabor Kato

As drugs and the complex biological entities on which they act are composed of molecules, their effect can accordingly be interpreted on the basis of molecular events. A drug may in fact itself be an endogenous substance, such as a neurotransmitter, but this does not change the general principle: its effect is governed by the interaction of drug or transmitter molecules on *receptor* molecules. The receptors are conceived, moreover, as being special structures within the molecular framework of cell membranes and cellular organelles. Such structures are capable of direct binding with specific, biologically active substances, and it is this binding that results in an observable physiological, pharmacological or biochemical response. Such a specific response can, of course, only be evoked by the interaction of very many molecules.

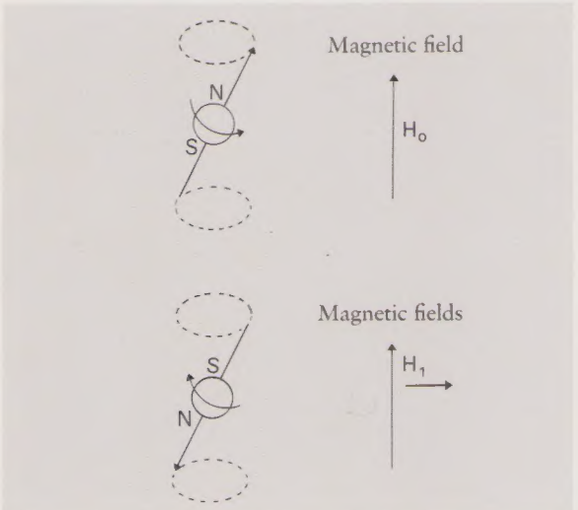
The pharmacological concept of receptors was first introduced by LANGLEY in 1905. He suggested that a pharmacological effect could only be produced by the action of the drug on a special receptive substance within the cell. Today it is widely supposed that the receptors are macromolecules – probably proteins – with structures resembling those of enzymes or antibodies. Many investigators believe that the receptors are located in the cell membranes. They almost certainly include structures sensitive to acetylcholine, epinephrine, histamine, serotonin and the peptide hormones. But whereas we know the chemical structure of most drugs, the structure of receptors is still a closed book.

The question arises as to why so little is known about the structure of receptor molecules. One major problem has been the lack of suitable methods for studying such molecules *in solution*. Until recently, the most direct method for deciphering receptor *activity* was by investigating the binding of a substance *within the tissues*, i.e. by determining the structures to which the substance is bound, and those of which the capacity to bind could be blocked by antagonists. But these methods only confirmed the occurrence of a reaction and neither indicated *how* these reactions occurred, nor *where* in the molecular sense. Complete answers to these ques-



'A classical definition of a pharmacologist given by Schmiedeberg was that of a man who investigates vital processes with the aid of chemical substances. For this to be accorded present-day validity, we must take into account certain basic changes in our conceptions at the turn of the century regarding the nature of vital processes. The insight gained into the chemical structure of living substances during recent decades has made it possible for us to consider life – as defined by Linus Pauling – as an interplay of forces taking place between molecules. This presents the pharmacologist with a new approach that goes far beyond a purely systematic study of the effect of drugs on intact living tissues, to which classical pharmacology was traditionally limited. The evolution of physical and chemical methodology have cleared a path for research into the laws underlying the specific character of pharmacology and has led to the foundation of the new sector of research – molecular pharmacology.' It would be difficult to find more fitting words than these of OLEG JARDETZKY for providing an introduction to an article of this type. They were written in the first place as an introduction to research on the action of drugs with the aid of NMR methods (appearing in *Naturwissenschaften* 54, No. 7, 1967). OLEG JARDETZKY is one of the pioneers in the application of the modern physical-chemical approach used by the author of this report in order to discover the acetylcholine receptor. The illustration shows a model of the acetylcholine molecule, the end of which fits into the troughs depicting the binding site on the hypothetical receptor in the postsynaptic neuronal membrane.

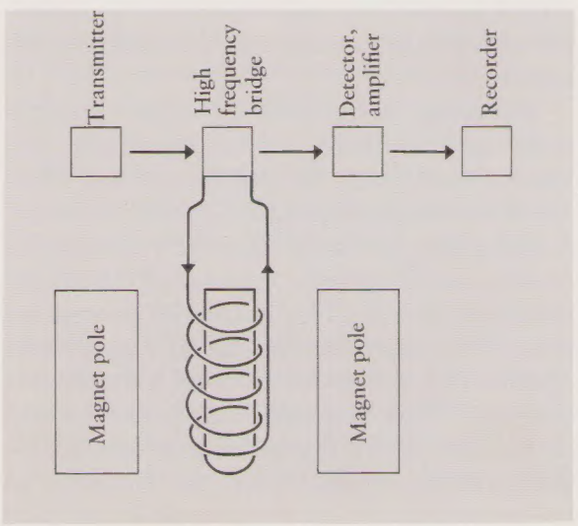
NMR spectroscopy is a method primarily concerned with hydrogen nuclei (protons). The nuclei of other elements can be observed too, but protons are especially suitable for molecular-biological studies since hydrogen constitutes a substantial part of all organic compounds. Thus the information obtained by proton spectroscopy provides a comparatively complete picture of the molecule being studied: the signal of each H atom in the spectrum is influenced by neighbouring atoms in a manner that can be interpreted in terms of specific molecular parameters. A strong magnetic field – H_0 – is used to align the protons which bear a positive charge and revolve about their own axis as if they were small magnets. According to the quantum theory the protons can assume one of two alignment positions, parallel or antiparallel, and their energy content will differ, depending on the alignment adopted. When a second, much weaker magnetic field – H_1 – is applied at right angles to H_0, a proton in the parallel alignment (low energy) can be made to turn over to the antiparallel (high energy) alignment. The field H_1 is formed by the magnetic part of an alternating high frequency electromagnetic field such as that produced by a radio transmitter. The protons can only 'flip over' if the energy of the radio frequency is exactly equal to the difference in energy between the two possible orientations of the proton. Hence the term 'resonance'. Since different protons within an organic compound exhibit slightly different resonance energies, the transmitter frequency has to be continually tuned. Whenever the frequency of the transmitter is equal to the resonance energy of a certain proton, this proton reverses its direction while absorbing energy. The energy absorbed is registered as a signal in the spectrum as a function of the transmitter frequency. Taking a nuclear magnetic resonance spectrum thus entails continuous variation of the transmitter frequency, i.e. varying the irradiation energy, and finding those values of energy which correspond to the resonance energies of particular protons in a molecule. The same effect is obtained by a simpler technique: the transmitter frequency – and hence H_1 – remains constant, while the strength of the magnetic field H_0 is varied. (The apparatus shown here is based on the latter principle.) It is evident that the stronger the magnetic field H_0, the greater will be the energy needed for the 'flip-over' – i.e. resonance energy is proportional to the strength of the magnetic field.

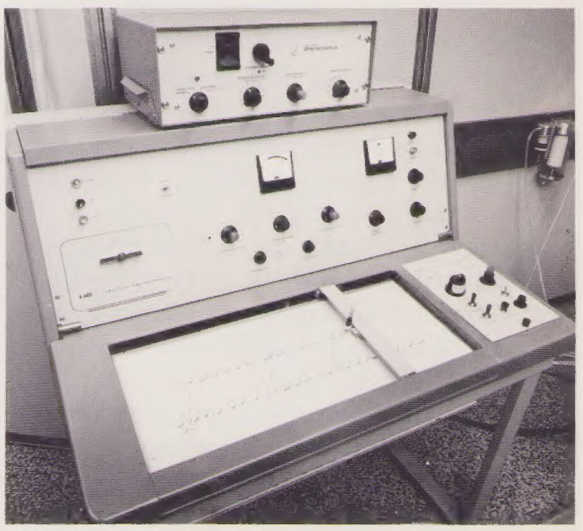


Under the guidance of Professor Krnjević, Director of the Department of Research in Anaesthesia at McGill University in Montreal, Dr. Gabor Kato tests a number of protein fractions obtained from nerve tissue in order to find out if they are possible acetylcholine receptors. A study employing NMR techniques is also being conducted in Montreal in order to determine the mechanism of action of the enzymatic inactivation of acetylcholine. It is hoped that one outcome of this work will be the discovery of new guidelines and data for developing new drugs.

The NMR equipment used here consists of the following elements: an electromagnet providing the field H_0, which may be varied within a certain range; a radio transmitter producing the resonance energy through a coil wound around the specimen; and a high frequency bridge which is able to measure the energy absorbed by the protons. The absorption signal is extremely weak and needs considerable amplification before it is fed to a chart recorder. The specimen to be tested in solution is in a small tube. If a solvent is used that normally contains hydrogen atoms, such hydrogen atoms must be replaced by deuterium as otherwise the signals of the solvent would interfere with the spectrum of the solute. The equipment shown here has a radio frequency of 60 MHz (megacycles per second) and a field strength of approximately 14 kGauss.

tions are only possible by studying solutions of both types of molecules, which in all likelihood form together an active biological complex. Smaller molecules – including drugs and endogenous substances – are relatively free to move in solution. There is in fact considerable relative mobility even between different parts of the same molecule. In the case of large molecules, however, of which receptors are most likely composed, there is a far lesser degree of mobility. Should a smaller molecule combine with a larger one, mobility of the smaller molecule, or at least part of it, is considerably reduced (i.e. that part which binds to the receptor). The applicability of *nuclear magnetic resonance*



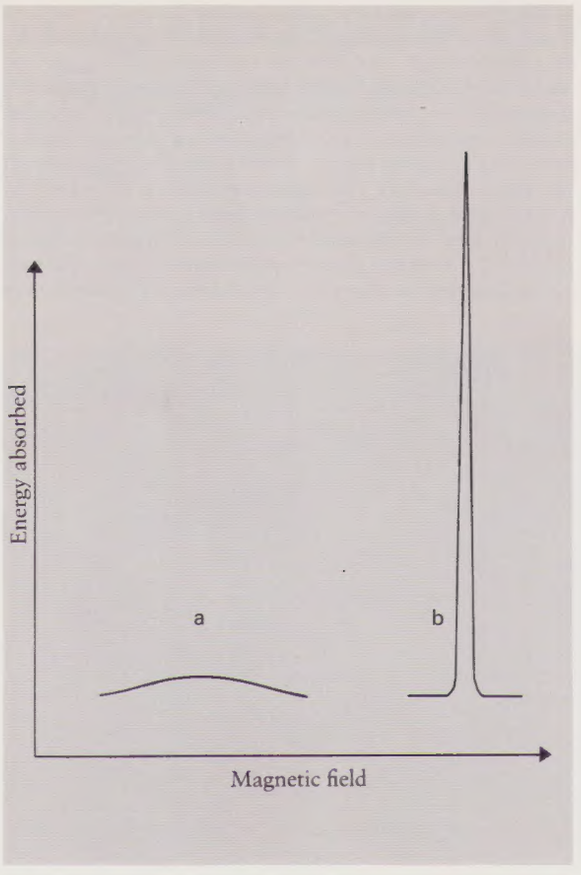


spectroscopy hinges on it being possible to measure a change of mobility of the individual chemical groups of the molecule. *How* this method is applied is explained in the illustrations.

There are two principal reasons why it is so important to know the structure of receptor molecules. The first may be explained by an analogy. If we understand the mechanism of a lock, for example, we should theoretically be able to make a key for it: similarly, if the structure of a receptor is known, we should be able to synthesize substances capable of reacting with it. We could for example develop an agent capable of interacting with a certain receptor with greater precision than existing drugs or transmitter substances. It might also be required to impede or promote the interaction between transmitter and receptor with such new substances. Knowledge of the exact site of action of both drugs and transmitters would be of great help to chemists and pharmacists in their search for new drugs.

The second reason may be explained by continuing the analogy. Provided its original structure is known, a defective or broken lock can be repaired or replaced. Or it may be possible to make a new key to suit a changed or modified structure of the lock. A well-known example of a faulty transmitter-receptor interaction is myasthenia gravis which may be treated by using a cholinesterase inhibitor. Certain forms of muscular dystrophy could also be the result of a similar disorder of biochemical mechanism and may one day respond to treatment made possible by receptor research. At present, however, it is impossible to define the extent to which the results of this line of research can eventually be applied.

Work in our laboratories is principally concerned with the study of the interaction between the neurotransmitter acetylcholine and the presumed receptor proteins. It is generally believed that acetylcholine produces this effect by combining with specific receptors located in the postsynaptic membrane. This reaction triggers a change in the permeability to ions in the postsynaptic cell

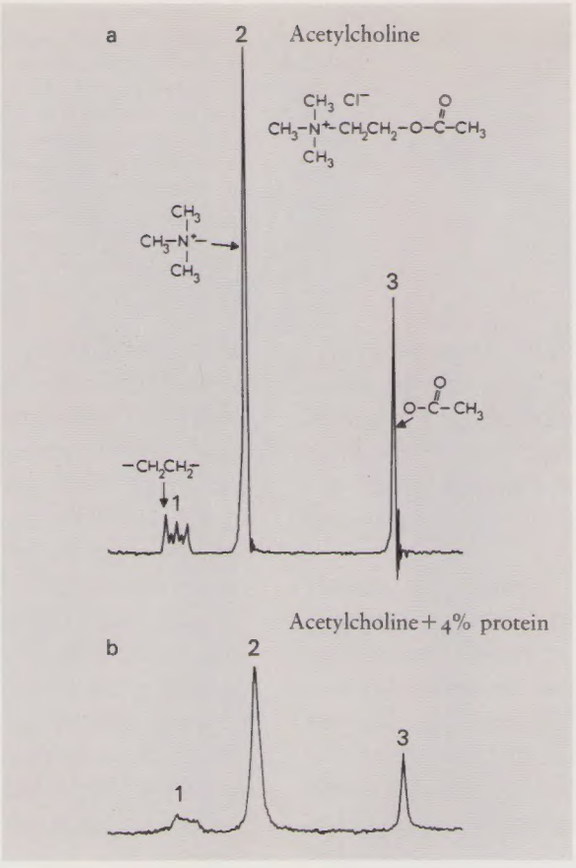


The applicability of NMR spectroscopy in the field of receptor-drug interaction hinges on the fact that the resonance peaks of freely moving molecules are much narrower than those of molecules with only limited mobility. Molecules of solids and of macromolecules give broad absorption peaks whereas small molecules in solution give sharp peaks. The primarily sharp signals of small molecules will be broadened by interaction with macromolecules, because the small molecule is now more or less fixed in a relatively rigid environment.

and the destruction of acetylcholine by a specific enzyme, acetylcholinesterase. We have attempted to extract such proteins from muscle, central and peripheral nervous tissue by chromatography and electrophoresis. The protein fractions obtained are concentrated and tested for their ability to bind acetylcholine and other cholinergic and anticholinergic drugs.

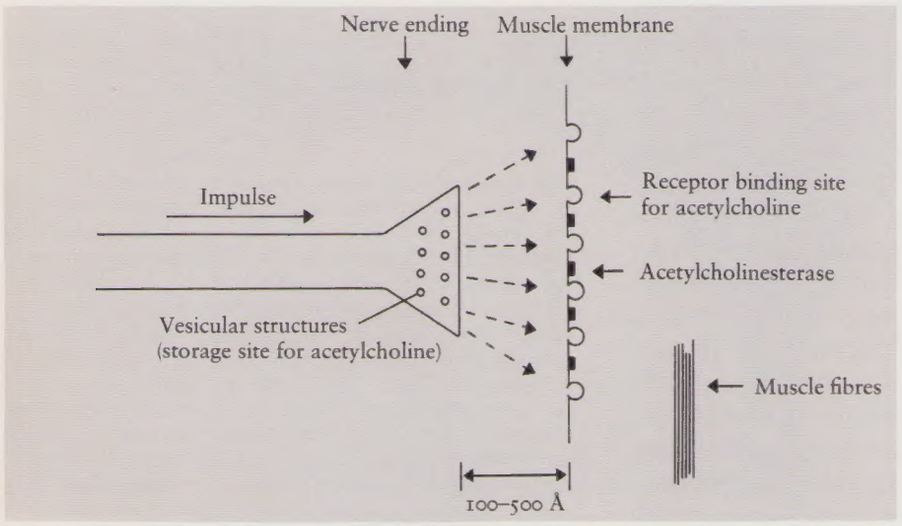
These fractions can be studied by first recording the nuclear magnetic resonance (NMR) spectrum of the acetylcholine or of a related or antagonistic test substance. This is followed up by adding the protein fraction and repeating the spectrum. Differences in the latter make it possible to conclude whether reaction has taken place or not, which part of the test substance has combined with the protein and the extent of the interaction.

Of some 30 purified proteins extracted from nervous tissue, only one (isolated from brain tissue) has so far had any marked effect on the resonance spectrum of acetylcholine. It had a clearly visible effect on reducing the mobility of all groups of atoms of the acetylcholine molecule. This particular protein reacts with acetylcholine in an apparently specific manner and it may be a membrane receptor. This conclusion is based on evidence that firstly the binding is specific for this protein, secondly that the binding can be prevented by anticholinergic drugs, and



If a small molecule interacts with a larger molecule, its mobility is considered restrained and the original resonance peaks of its H atoms are broadened. If the entire molecule interacts, all its resonance signals are affected. If only a special group of the molecule is bound to the macromolecule, the protons of this group will have reduced mobility and will give broader lines. Other signals remain unchanged. In this manner the researcher obtains information on which part of the small molecule from the binding site of the macromolecule will actually be bound and form the active complex. The spectrum of a solution of acetylcholine shows a sequence of sharp signals which relate individually or in groups to particular H atoms of the molecule. The fine structure visible in the illustration reflects the mutual influence of various protons within the molecule. After a certain protein fraction extracted from brain tissue is added, all signals are broadened due to the specific receptor properties of this protein fraction for acetylcholine.

Hypothetical mechanism of neuromuscular transmission. Motor impulses arriving at the nerve ending induce the release of acetylcholine stored in the vesicular structures of the presynaptic membrane. Acetylcholine molecules then traverse the narrow gap to combine with the receptor sites on the muscle membrane and the muscle fibres contract.



thirdly that other drugs not related to acetylcholine do not interact with the protein. Recordings taken of the time of the interaction indicate that the acetylcholine-protein complex only exists for a few seconds. This is particularly relevant since there is every reason to believe that the acetylcholine-membrane interaction is also merely transient in living tissues.

The next phase of research is purifying the possible receptor protein in order to investigate its size, structure and binding sites. By this method we hope to isolate and identify the receptor molecule with which acetylcholine reacts.

The second aspect on which our laboratory is concentrating is the mechanism of interaction between acetylcholine and acetylcholinesterase, the enzyme which hydrolyzes acetylcholine into choline and acetate. This interaction is also transient owing to the destruction of acetylcholine by the enzymes. The more acetylcholine is broken down, the fewer are the molecules available for binding. Furthermore this interaction can be prevented by anticholinesterases such as physostigmine, neostigmine and edrophonium, which compete for the active site and therefore prevent hydrolysis of acetylcholine. Information obtained on the interaction between acetylcholine and the enzyme breaking down the transmitter is by no means of purely theoretical interest. Several investigators believe that acetylcholinesterase may itself be the receptor for acetylcholine.

Art Forms in Nature

Raoul Zingg

The author and editors dedicate this article on Ernst Haeckel to the memory of Max Breitschmid who died on November 12, 1970. From the founding of IMAGE *up to about two years ago, Max Breitschmid was responsible for the layout of our magazine. His rich store of knowledge and scholarly background constantly enabled him to make interesting suggestions and cultivate contacts with artists, scientists and collectors, with whom common interests and personal leanings had forged firm bonds during his full cultural life. We are in fact indebted to Max Breitschmid for his idea to publish this study on Art Forms in Nature.*

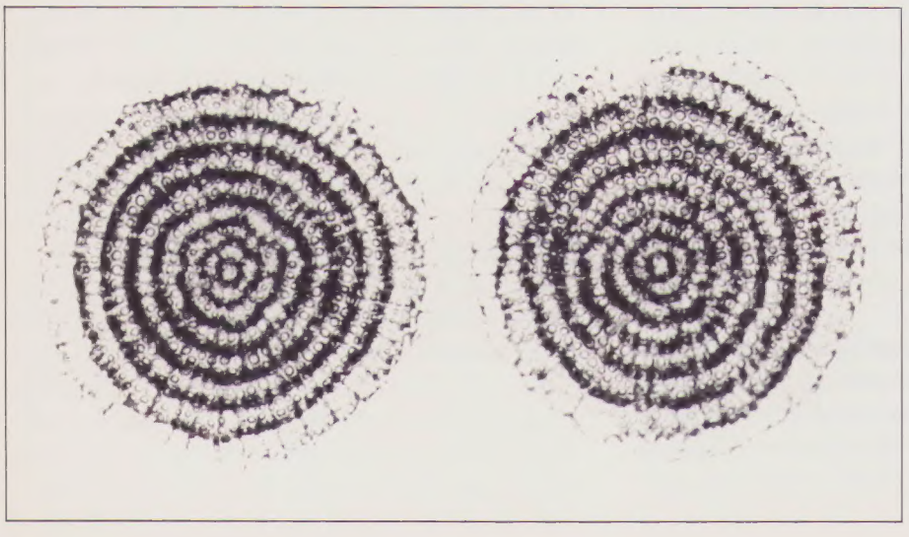
This was the title chosen by Ernst Haeckel, Professor of Zoology at Jena, for his illustrated work which is undoubtedly unique of its kind. Appearing in ten parts published between 1899 and 1904, it consists of exceptionally fine paintings of protozoan organisms.

Revered by many, reviled by some, Haeckel was, at least in German-speaking circles, doubtless one of the most fascinating figures of the turn of the century. An unquestionable authority on zoology, he not only propagated Darwin's doctrine of evolution but tried to apply it in drafting out a new system of biological classification. This necessitated a study on man's descent which he regarded as a particular development taking place within nature in its entirety. Haeckel's opponents repudiated this important opinion as consistently as they attacked the alleged doctrine of Darwin that the human race was descended from the ape. In point of fact, however, both Darwin and Haeckel spoke merely of the relationship between man and the great apes as the end links of a line of evolution, which, although having taken two separate ways, springs from a common root. This conception of the relationship had caused Linnaeus (1707–1778) to enter man and anthropoids alike under the order of Primates in his *Systema naturae*. Zealous champion of this conception, Haeckel belongs to the 'fathers' of a scientific theory on the origin of the species. The mass of material offering itself to the researcher permitted only one initial classification or attempt at interpretation. Even Haeckel was unable to relate theory and hypothesis within the framework of his research, although he was often aware of the doubtful nature of these intellectual 'auxiliary constructions'. Indeed, in its original form his fundamental biogenetic law is no longer valid. The same applies to his *Gastraea* theory, although both of these doctrines were of fundamental significance as working hypotheses – or rather, 'thinking' hypotheses.

For Haeckel no gap existed between inorganic and organic natural substances: he

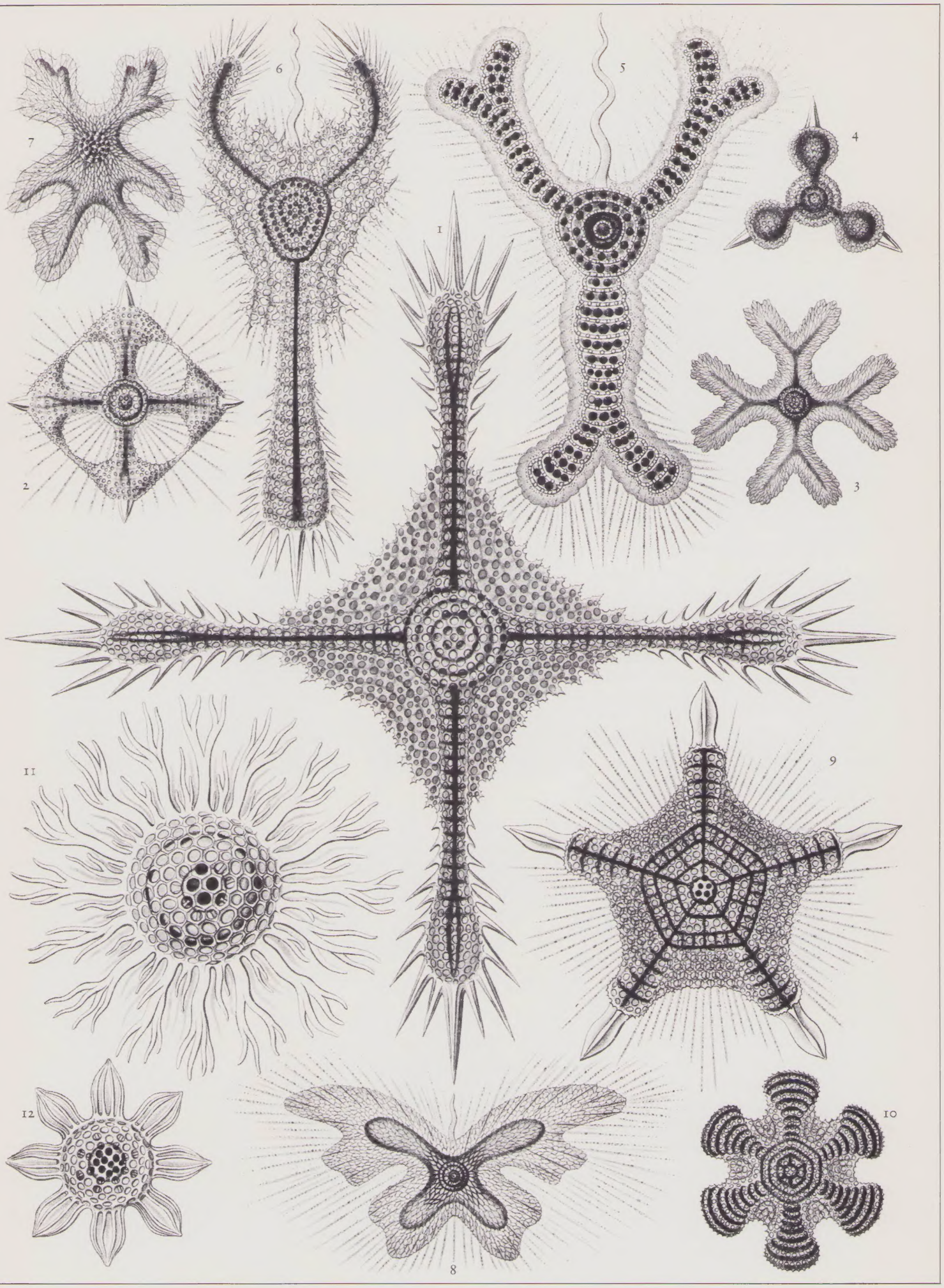
Stylodicta spc.
(tropical Atlantic).

Porodiscus spc.
(tropical Atlantic).



1. *Histiastrum Boseanum* (Haeckel). ▸
2. *Stephanastrum quadratum* (Haeckel).
3. *Dicranastrum furcatum* (Haeckel).
4. *Rhopalastrum trispinosum* (Haeckel).
5. *Chitonastrum lyra* (Haeckel).
6. *Euchitonia carcinus* (Haeckel).
7. *Myelastrum dodecaceros* (Haeckel).
8. *Myelastrum papilio* (Haeckel).
9. *Pentinastrum asteriscus* (Haeckel).
10. *Hexinastrum geryonidum* (Haeckel).
11. *Heliodrymus dendrocyclus* (Haeckel).
12. *Heliodiscus glyphodon* (Haeckel).

The Radiolaria are marine planktonic protozoa occurring in neritic, pelagic and bathypelagic waters. These minute animals with radiating spicules constituted Haeckel's favourite objects of study. Beautiful skeletal structures are formed by the secretory activity of radiolarian protoplasm. Such structures are frequently of the lattice type which, in addition to being extremely intricate, are specific for particular species. The skeleton is usually of silica, but some species also form an agglutinated capsule from the remains of diatom shells, smaller radiolarians and other material. A large variety of skeletal elements protruding from the central capsule serve as a hydrostatic mechanism. The protoplasm is composed of inner (entoplasm) and outer (ectoplasm) constituents. The inner cytoplasm is divided into a central portion surrounded by a capsule and containing the nucleus or nuclei, fat droplets, albuminous crystals and pigment granules. Separated from the entoplasm by a membrane is the extracapsular cytoplasm, or calymma, which consists of multi-layered ectoplasm and gelatinous envelope. The ectoplasm contains inclusions of nutrient vacuoles, food remains and pigments; from it radiate the numerous pseudopodia from which this order of rhizopods derive their name. The ectoplasm of radiolarians in illuminated zones also contains symbiotic zooxanthellae, single-celled algae. Radiolarians generally multiply by binary fission – usually involving the skeleton, the daughter cells subsequently restoring the missing skeletal elements. In the case of groups having intricate skeletal structures, one daughter remains in its original housing, while the other deposits a new skeleton. In some cases, sexual reproduction has been observed in addition to the asexual methods just described. In spite of the numerous studies carried out on these animals, a complete classification has still not been drawn up, neither for their phylogenetic nor for their ontogenetic skeletal evolution, although the phylogenic origin of the forms is largely known in some orders.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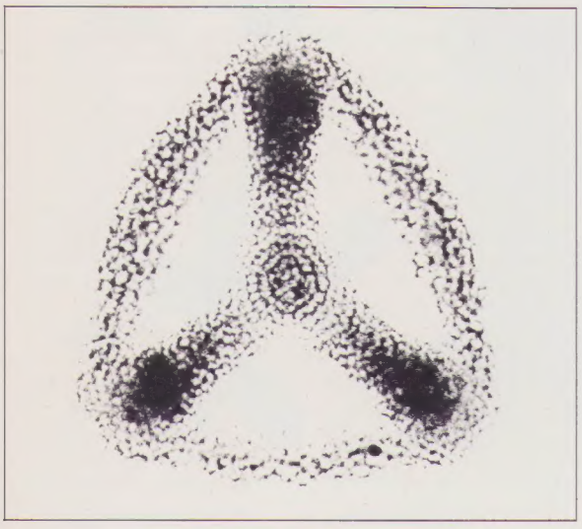
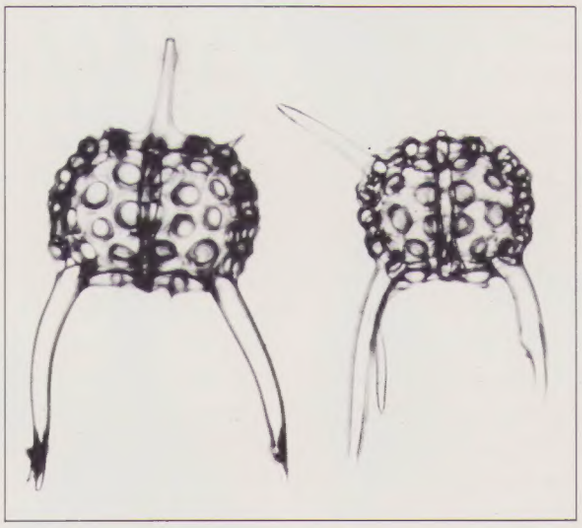
Euchitonia mülleri Haeckel (H.), var. grottensis, fossil (Caltanisetta, Sicily).



Dendrospyris dirhiza (Ehr.) H., fossil (Barbados).

Aegospyris longibarba (Ehr.) H., fossil (Barbados).

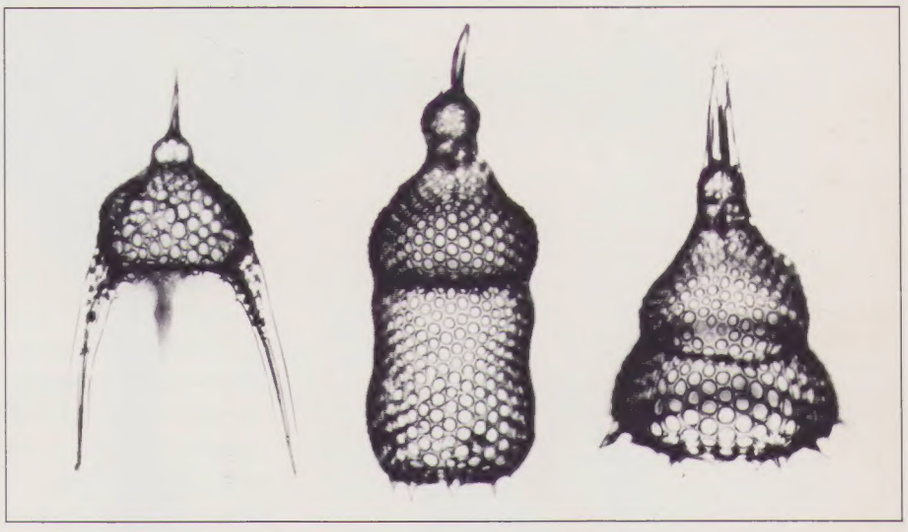


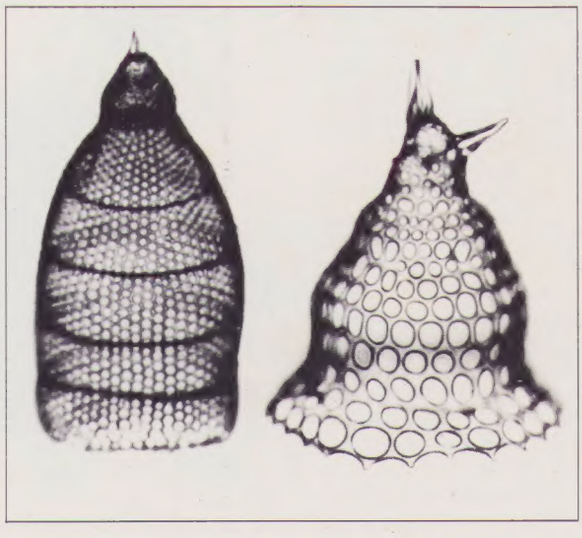
Pterocanium tricolpum H. (Indian Ocean).

Calocyclas amicae H. (Indian Ocean).

Lamprocyclas martialis H. (Indian Ocean).

▼



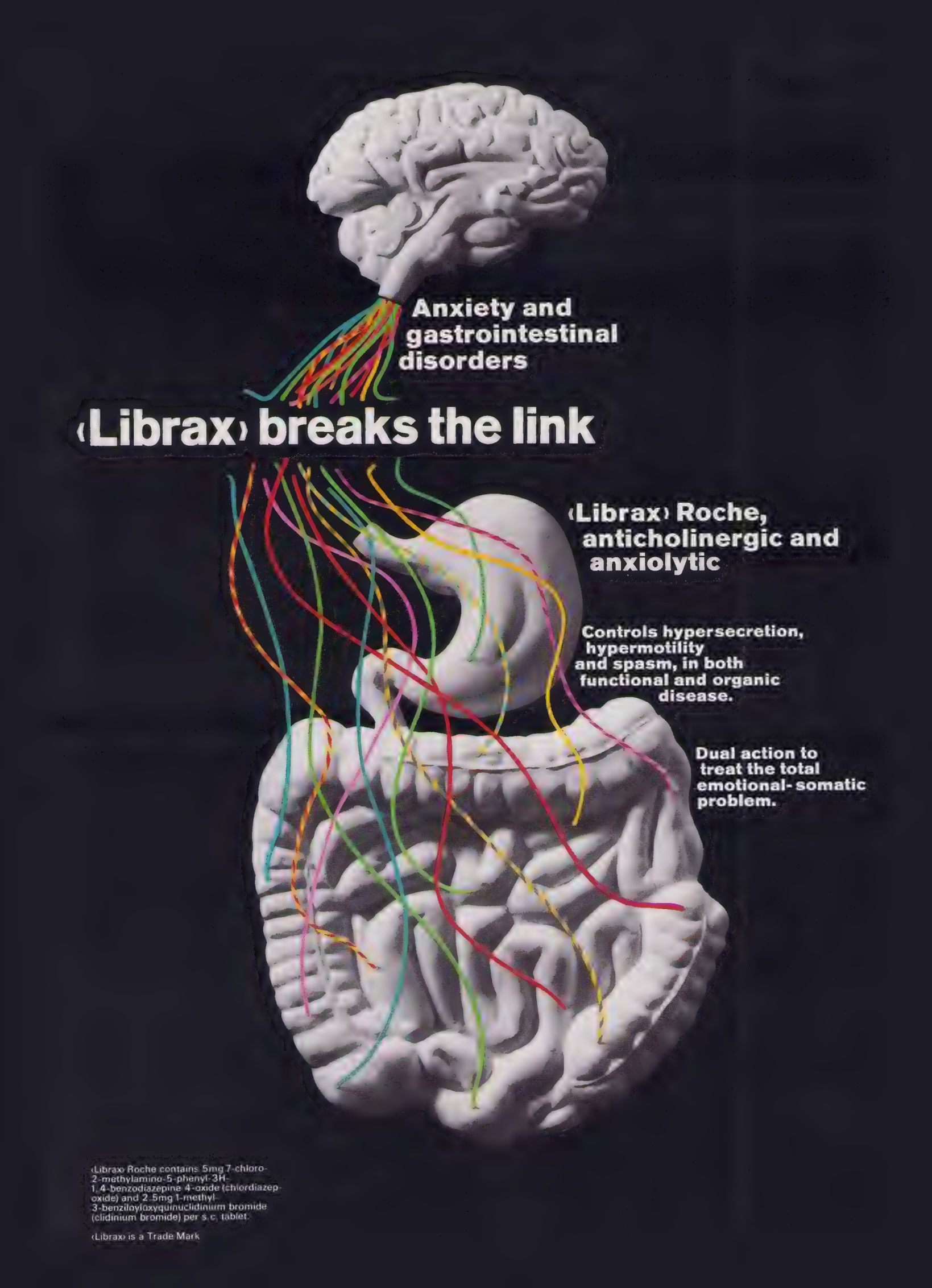


Eucyrtidium cienkowski H. (Indian Ocean).

Clathrocyclas semeles H. (Indian Ocean).

asserted their essential unity governed by the laws of nature. Yet in the light of recent successes in biochemical and biophysical research (part synthesis of nucleic acid from inorganic raw materials with the aid of ultraviolet) even this conception acquires a modern ring.

At no time have workers in scientific research been infallible. This has been shown by the support given by the paleontologists Agassiz and Cuvier to the doctrine of the fixity of species and Cuvier's catastrophe theory of geologic formations. Yet it would still be unwise to belittle the magnificent achievements of these researchers. Virchow's judgement on the first findings of fossilized human remains may have been wide of the mark, but even this cannot alter the fact that he was one of the greatest pathologists of all times. *Errare humanum est*. But it seemed that Haeckel was to be doubly debited with every mistake, whether actual or alleged. This was perhaps because the great Jena zoologist, passionate champion of Darwin's theory of the origin of the species by natural selection, did not write and lecture for merely a small circle of learned colleagues. Convinced of the importance of scientific knowledge for the well-being of mankind, he turned, with nothing short of missionary zeal, to a wide sector of the population. Haeckel's adversaries, recruited for the most part from orthodox ecclesiastical circles thus found them-


Anxiety and gastrointestinal disorders
‹Librax› breaks the link
‹Librax› Roche, anticholinergic and anxiolytic
Controls hypersecretion, hypermotility and spasm, in both functional and organic disease.
Dual action to treat the total emotional-somatic problem.

‹Librax› Roche contains 5mg 7-chloro-2-methylamino-5-phenyl-3H-1,4-benzodiazepine 4-oxide (chlordiazepoxide) and 2.5mg 1-methyl-3-benziloyloxyquinuclidinium bromide (clidinium bromide) per s.c. tablet.

‹Librax› is a Trade Mark

‹Valium› Roche

(diazepam) contains as active substance 7-chloro-1, 3-dihydro-1-methyl-5-phenyl-2H-1, 4-benzodiazepin-2-one

TABLETS & SYRUP:
N.H.S. RESTRICTED BENEFIT
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From worry to worse

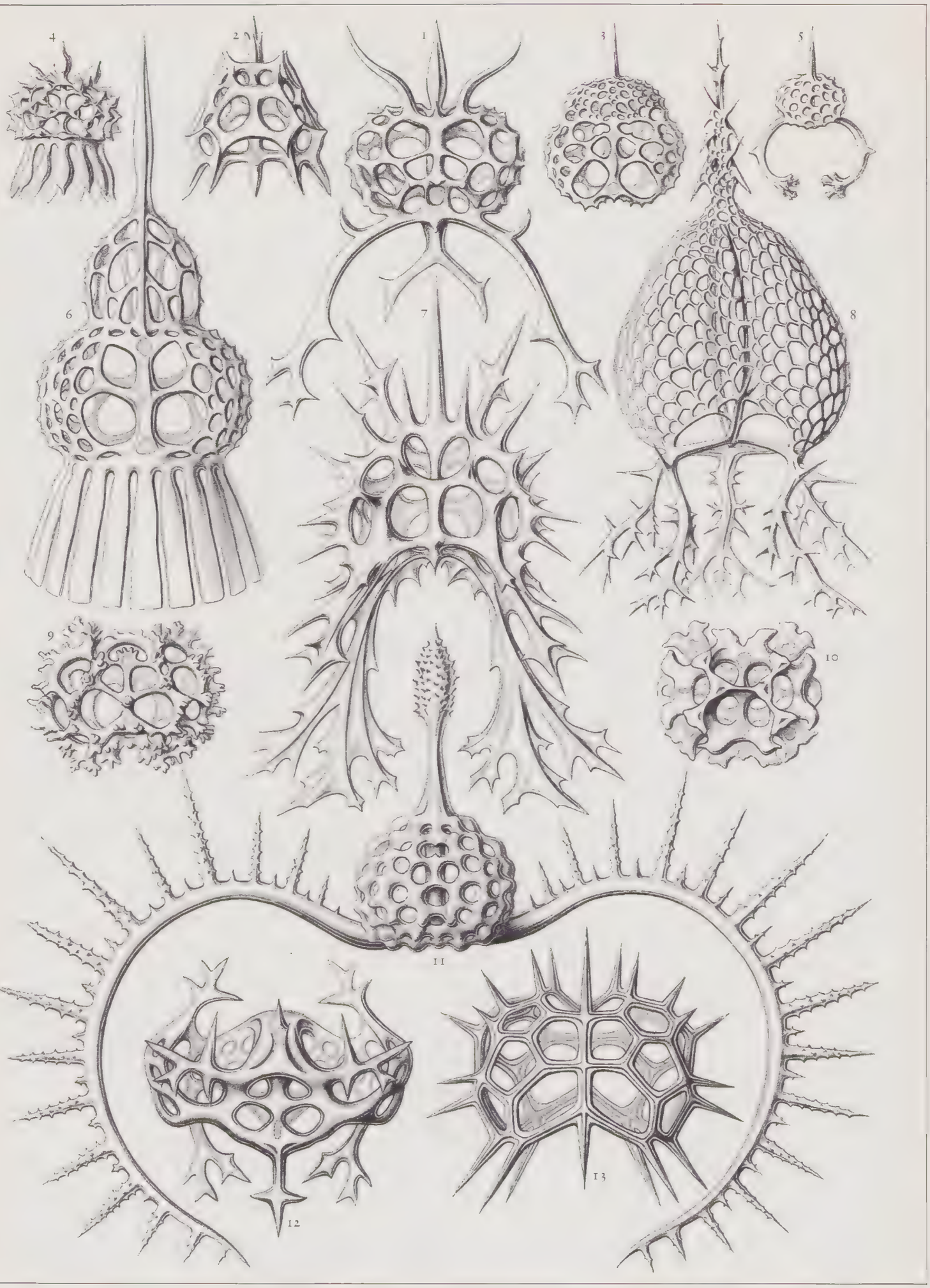
Thanks to research in neurophysiology, neuropharmacology and psychology we have now mapped every nook and cranny of the road which starts with emotional disturbance.

We are now aware of the vital importance of the limbic system as the substrate of the emotions—its direct relationship, through the hypothalamus, with the autonomic and hormonal systems. . .

‹Valium› Roche, through its finely balanced effect on this emotional substrate, effectively treats not only emotional irregularities but also emotionally-conditioned functional disorders and organic lesions.

Indications: All illnesses which give rise to emotional tension, anxiety, excitation, restlessness, hypochondriac tendencies; headaches, cardiovascular, broncho-respiratory, gastrointestinal and urogenital disorders caused by emotional imbalance; centrally or peripherally determined muscular spasm.

‹Valium› Roche is a Trade Mark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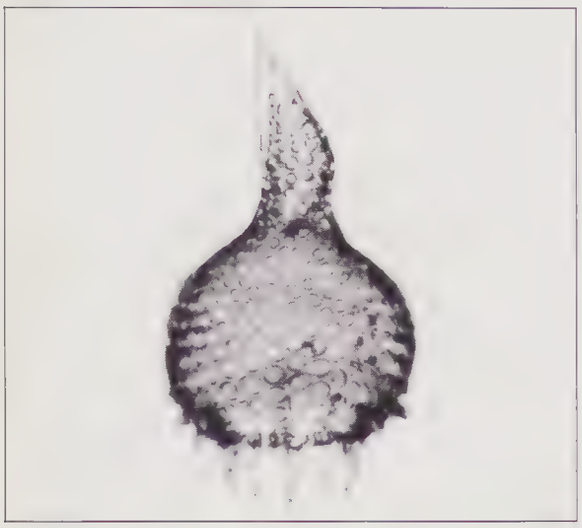
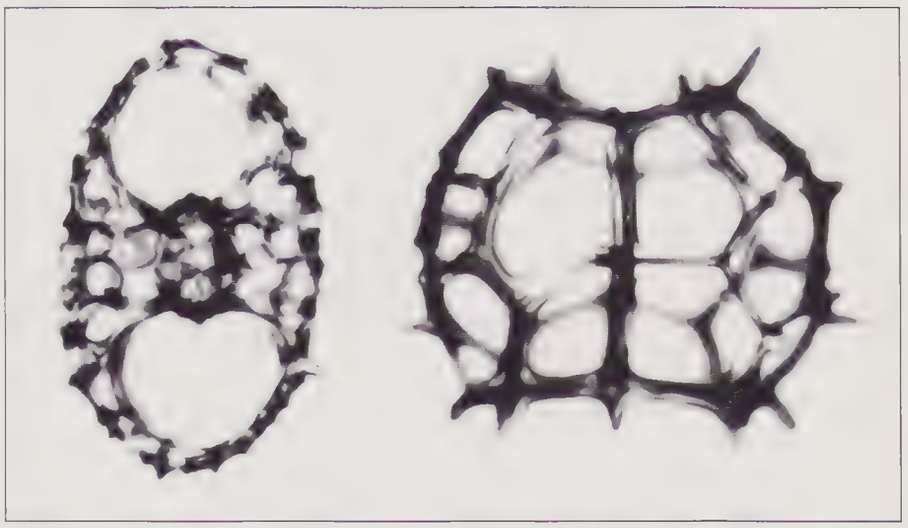
1. *Cyrtophormis spiralis* (Haeckel).
2. *Clathrocanium reginae* (Haeckel).
3. *Anthocyrtium campanula* (Haeckel).
4. *Pterocorys rhinoceros* (Haeckel).
5. *Lithornithium falco* (Haeckel).
6. *Alacorys Bismarckii* (Haeckel).
7. *Calocyclas monumentum* (Haeckel).
8. *Pterocanium trilobum* (Haeckel).
9. *Stichophaena Ritteriana* (Haeckel).
10. *Dictyocodon Annasethe* (Haeckel).
11. *Artopilium elegans* (Haeckel).

selves directly involved. A scarcely ever-contested notion backed by an eighteen-hundred-year belief of man's central terrestrial and cosmic position was threatened with obsolescence. Emotional reasons, reaction to anthropogenesis which inevitably showed a trail leading back to the animal, moved other contemporaries to eschew Haeckel's outlook. What started off as a grapple between the new doctrine of natural science and the sacred doctrines of tradition turned unexpectedly into a struggle of dogma against dogma carried on without even a trace of fairness. It should not be forgotten that Haeckel's monistic attitude increasingly acquired the nature of a universal philosophy. Buth this dispute soared to a new crest of crassness when a limitation was imposed on teaching and associations. The restriction was demanded by the scientist Reinke before the Prussian Upper House in 1907 and was undoubtedly directed against Haeckel and his monistic league. Police-state methods were to protect church and school, throne and altar from these 'revolutionaries'. Yet the bitter struggle proved pointless; theologists and associates of both confessions lost more and more ground. Even if in modified form, Darwin's theory of evolution propagated by Haeckel was to show itself the stronger in spite of all the 'death wishes', dismal prophecies and polemic levelled against it.

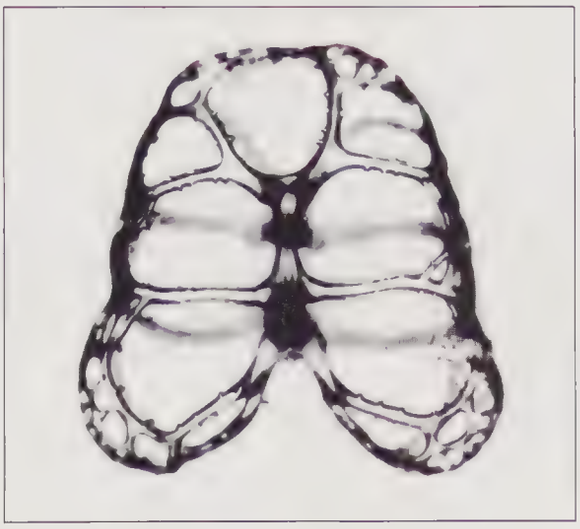
Sethoconus clathratus (Ehr.) H.
(tropical Atlantic).



Anthocyrtium ehrenbergi H. (tropical Atlantic).



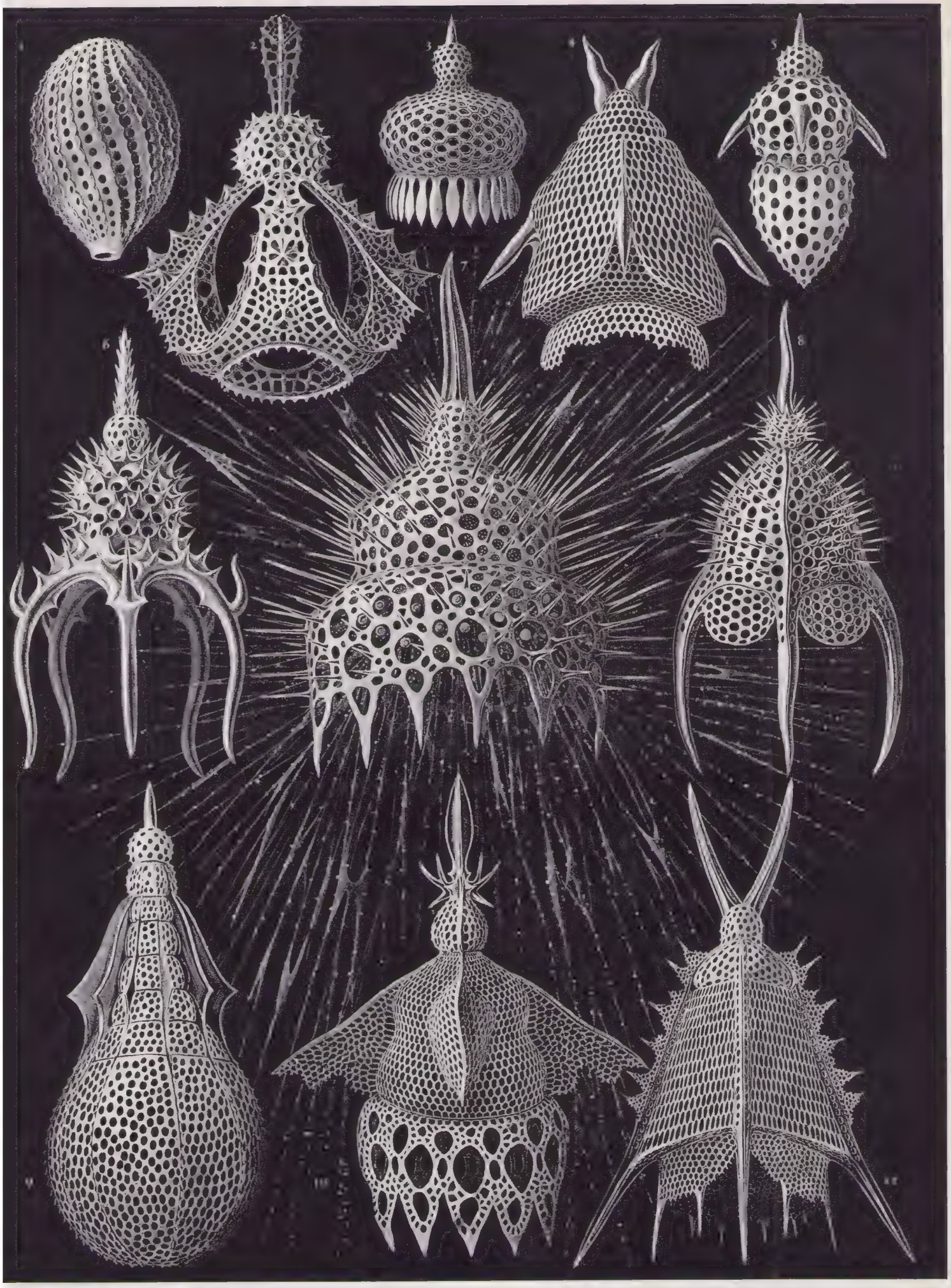
Tetrapyle spc.



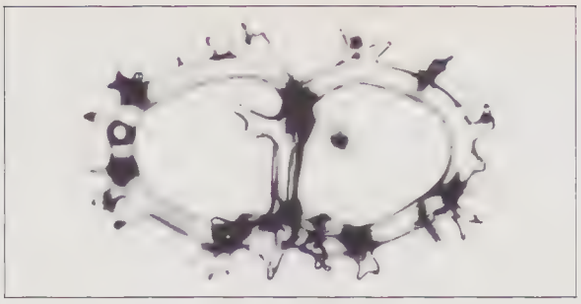
Ceratospyris allmersi H.
(Allmers, poet and friend of Haeckel)
(Indian Ocean).

1. *Triceraspyris gazella* (Haeckel).
2. *Clathrospyris pyramidalis* (Haeckel).
3. *Pylospyris canariensis* (Haeckel).
4. *Anthospyris mammillata* (Haeckel).
5. *Dendrospyris polyrrhiza* (Haeckel).
6. *Sepalospyris pagoda* (Haeckel).
7. *Elaphospyris cervicornis* (Haeckel).
8. *Tholospyris cupola* (Haeckel).
9. *Dictyospyris stalactites* (Haeckel).
10. *Dictyospyris anthophora* (Haeckel).
11. *Dorcadospyris dinoceras* (Haeckel).
12. *Triceraspyris damaecornis* (Haeckel).
13. *Ceratospyris Strasburgeri* (Haeckel).

Amphispyris sternalis H.
(Indian Ocean).

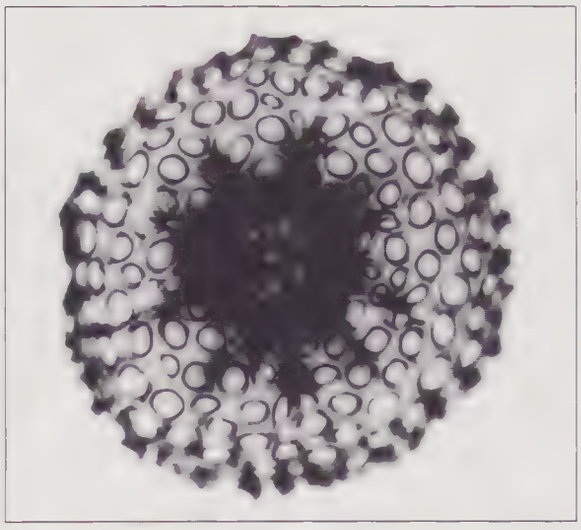


Tristephanium hertwigi (Bü) H., fossil (Barbados).

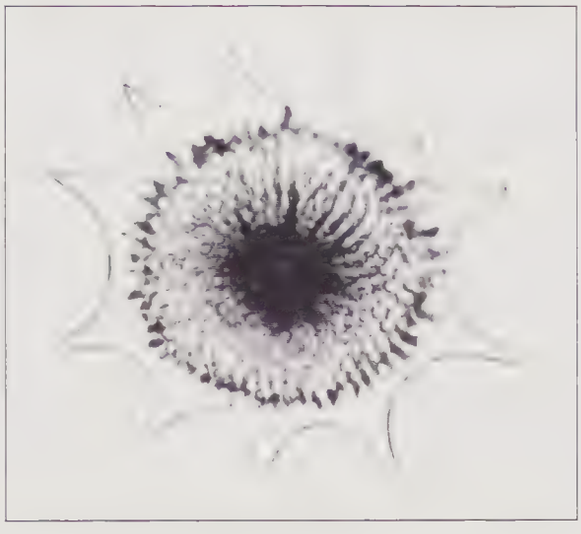


Let us turn from Haeckel the controversial Darwinian to Haeckel the accepted zoologist; the Haeckel that in extensive monographs on calcareous sponges, radiolarians and medusae introduced more than four thousand new species; the Haeckel that guided the further research of his students and followers; and finally, the Haeckel that singled out marine plankton, especially radiolarians, as the objects of his most devoted attention.

It is hard to name an area in which he did *not* find material for examination. He appeared 'at home' in most of the seven seas, be it the Mediterranean, the Red Sea, the North Sea or the Pacific Ocean. In addition to his expeditions he also produced many works of popular scientific interest. With *Kunstformen der Natur* (Art Forms in Nature) it was his intention to introduce to 'an extended circle of artists and those interested in the natural sciences the hidden features of the organic world, which, in the lower orders of the animal and vegetable kingdoms, has developed into a little-known realm of fascinating form and beauty'. (Quoted from a covering letter, sent by Haeckel with the first part of his work to all those who had celebrated his 60th birthday with him a few years previously.)



Heliodiscus astericus H., fossil (Caltanisetta, Sicily).



Astrosestum octogonium Br., fossil (Barbados).

The work fulfilled all expectations. Scarcely any publication of that time had made a greater contribution to representing so strikingly the unique beauty of such hitherto elusive marine organisms. The work also provided stimulus for the studies of enthusiastic amateur microscopists, many of which had proved extremely rewarding. *Kunstformen der Natur* even served as a pattern for the arts and crafts of the *Art Nouveau* epoch. Forms from the world of the diatoma, algae and many other groups appeared engraved or stamped in metal, cut in glass or printed and embroidered on fabrics – just as the designs of some present-day ceramics draw on illustrative works of flowers or butterflies for their motifs. The ten volumes of Haeckel's work include 100 full-page plates, descriptive texts and taxonomic detail. Today, the plates are no longer considered to be all of equal value. Illustrations of turtles, frogs, reptiles and antilopes appear somewhat stiff, although they are never incorrect. Compositions, such as the plate illustrating mosses and ferns, reflect the style of the times. But on observing closely the many plates depicting marine forms of the plankton world – which can only be seen under the microscope – it becomes evident that a searching eye has guided the trained hand of an artist with a style of his own. The plates of radiolarians, foraminifers, sponges, medusae, peridiniums, diatoms, ciliates or flagellates are plainly magnificent works of art obviously executed with great dedication.

Profile of progress

Name Mrs. Raynor Reference Number —

Depression Evaluation Chart

Pre-treatment — 2nd Evaluation +2 3rd Evaluation +6

Symptoms	absent	mild	mod.	severe	absent	mild	mod.	severe	absent	mild	mod.	severe
Agitated	0	1	2	3	0	1	2	3	0	1	2	3
Tense and irritable	0	1	2	3	0	1	2	3	0	1	2	3
Unable to get to sleep	0	1	2	3	0	1	2	3	0	1	2	3
Lost appetite	0	1	2	3	0	1	2	3	0	1	2	3
Has wind, indigestion, palpitations, urinary frequency	0	1	2	3	0	1	2	3	0	1	2	3
Pessimistic attitude	0	1	2	3	0	1	2	3	0	1	2	3
Thinks and acts more slowly	0	1	2	3	0	1	2	3	0	1	2	3
Has suicidal ideas	0	1	2	3	0	1	2	3	0	1	2	3
Self-reproach, guilt	0	1	2	3	0	1	2	3	0	1	2	3
Gets tired and exhausted	0	1	2	3	0	1	2	3	0	1	2	3
Wakes early	0	1	2	3	0	1	2	3	0	1	2	3
Suspicious	0	1	2	3	0	1	2	3	0	1	2	3
Lost interest in sex	0	1	2	3	0	1	2	3	0	1	2	3
Lost interest in social activities	0	1	2	3	0	1	2	3	0	1	2	3
Preoccupation with health	0	1	2	3	0	1	2	3	0	1	2	3
Has constipation, headache, backache, other somatic symptoms	0	1	2	3	0	1	2	3	0	1	2	3
	Total	21			Total	10			Total	5		

ROCHE

Laroxyl

amitriptyline lifts depression

N.H.S. General Benefit

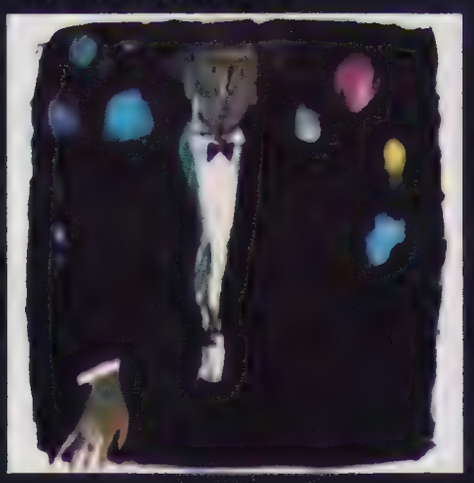
	Max. Qty.	Rpts.
Tablet 10 mg	100	2
Tablet 25 mg	100	2
Amps. 50 mg/2 ml	10	Nil

Roche Products Pty. Limited, Sydney

Laroxyl — Trade Mark

The 'hypertensive' patient

The 'heart' patient



The 'skin' patient

The 'rheumatic' patient

The 'headache' patient

The 'gastric' patient

Patient care in general practice

‹Valium› Roche

(diazepam)

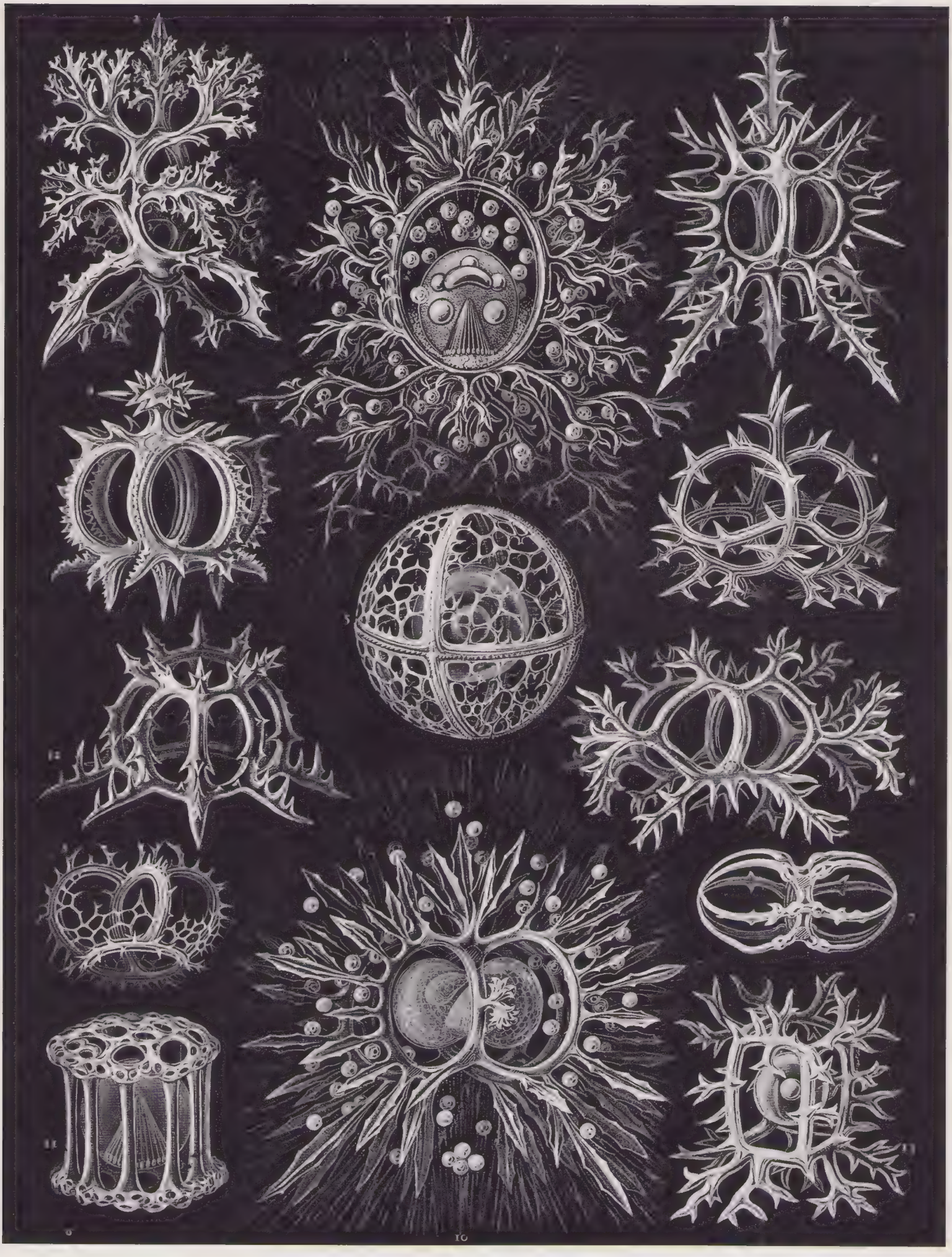
more than a tranquilizer

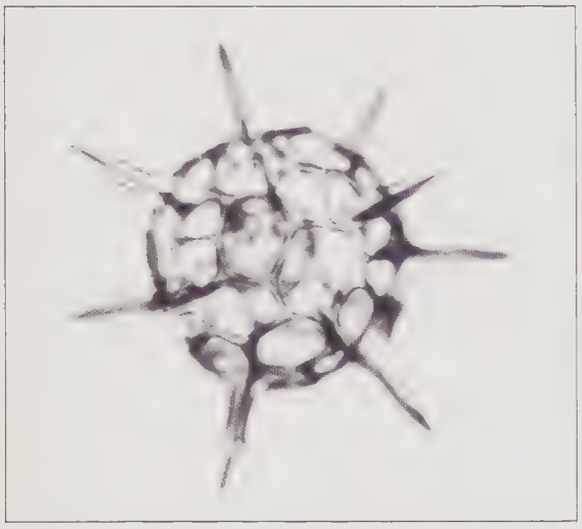
TABLETS & SYRUP:
N.H.S. Restricted Benefit
as listed—also
full Pensioner Benefit
AMPOULES:
N.H.S. General Benefit

ROCHE

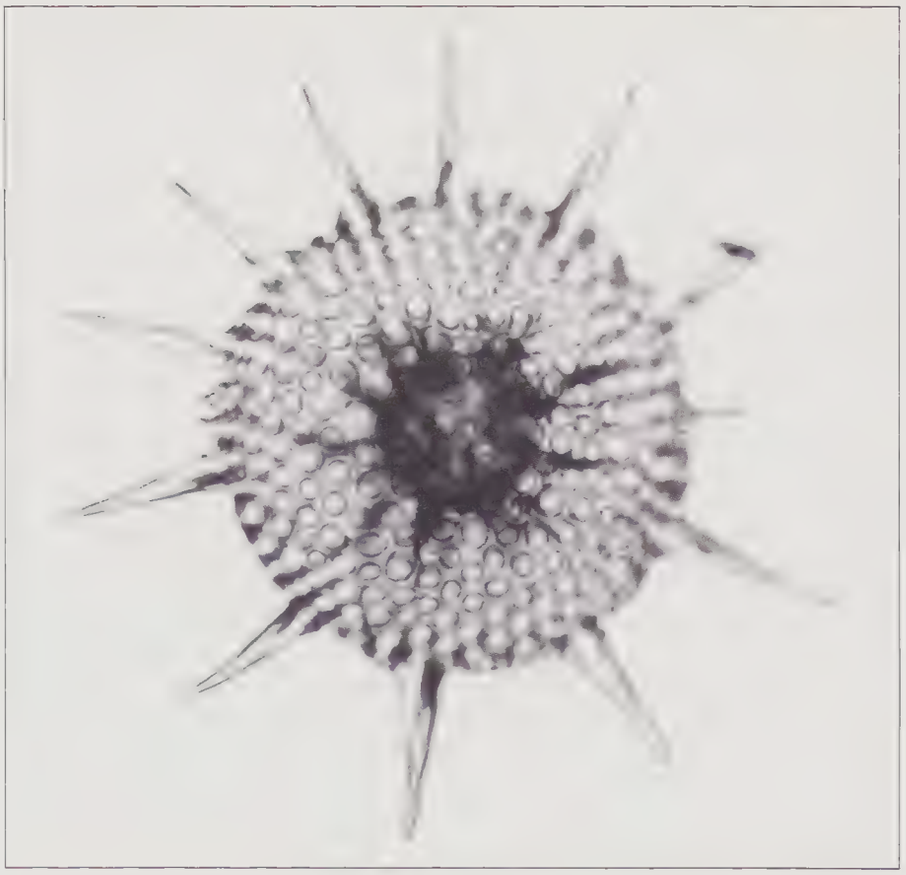
Roche Products Pty. Limited, Sydney

Valium Roche = Trade Mark





Echinoma elegans Br. (Indian Ocean).



Heliodiscus astericus H. rez. (Indian Ocean).

The scope of this article is limited to introducing radiolarians. The foraminifers, diatoms, desmids, peridiniums and flagellates will be dealt with in a subsequent article.

The microphotographic shots shown for comparison do not always correspond to the species selected by Haeckel. This is intentional as, firstly, some of those selected by Haeckel are not always easy to come by; secondly, it has thus been possible to widen the scope of *Art Forms in Nature* and heighten the overall effect. A comparison of the illustrations from the plates with corresponding microphotographs shows the significance a skilled drawing has even today. The draughtsman is able to interpret and depict the whole object, while, owing to its small depth of field, even the weakest of microscopes just covering resolution requirements can only show part of the object.

◂ 1. *Lithocircus magnificus* (Haeckel).
2. *Semantis sigillum* (Haeckel).
3. *Acanthodesmia corona* (Haeckel).
4. *Tristephanium dimensivum* (Haeckel).
5. *Trissocyclus sphaeridium* (Haeckel).
6. *Octotympanum cervicorne* (Haeckel).
7. *Microcubus zonarius* (Haeckel).
8. *Tympaniscus tripodiscus* (Haeckel).
9. *Tympaniscus quadrupes* (Haeckel).
10. *Tympanidium foliosum* (Haeckel).
11. *Lithotympanum tuberosum* (Haeckel).
12. *Circotympanum octogonium* (Haeckel).
13. *Lithocubus astragalus* (Haeckel).

It should be stressed here that the species given by Haeckel are now partly included under other genera or families.

We should like to thank Mr. G. Jaccard, Basle, for kindly submitting his fine radiolarian and Foraminifera preparations for microphotography.

CARTOONS

Marcel Vertès was born in Ujpest, Hungary, in 1895. The initial stimuli destined to play such a decisive role in the development of his art were acquired in Paris, where he settled in 1920 and experienced his first success a year later. The breakthrough came when Forain, then president of the *Salon des Humoristes*, retained the entire twenty-five water colours Vertès had sent in. The artist came mainly under the influence of Degas and Toulouse-Lautrec – in 1952 he designed the decor and costumes for the film 'Moulin Rouge'. He also illustrated books by Colette, Francis Carco and Pierre Louÿs. After the capitulation of France in 1940 he was demobilized from the army, in which he had served as a reservist, and left for the United States. France and North America are in fact the countries in which he exhibited his work, decorated hotels and theatres and published books up to his death in 1961. The following drawings are taken from the book entitled *It's All Mental*. New York:Tudor 1948.

'Oh doctor, you've given me back my self-confidence!'

'Your analysis is terminated... from now on you're a happy man!'

'That was a good one!'

'Thanks a million, doctor, for making a man out of me!'

'And now, tell me everything about myself.'

'Have you a couch where I could try it for effect? I want it to wear when I visit my analyst.'

'... born 1769 in Ajaccio, son of Carlo and Letizia Buonaparte...'

'As your father happens to be an old friend of mine, I'm treating your case as an exception... when you get home take a couple of aspirins and everything will work out fine.'

COLOR IMAGE

Among the Ajoré Indians of the Gran Chaco

Ulf Lind

Attempts by civilization to penetrate the northern part of the Gran Chaco have met with stubborn resistance. These regions have not so far been reached by the waves of settlers comprised of Bolivians from the Andes and Paraguayans from the eastern bank of the Rio Paraguay. It is estimated that some six hundred Ajoré tribesmen still roam the swampy lands flanking the confluence of the Rio Otuquis with the Rio Paraguay, the lands bordering the salt lakes on the Bolivian-Paraguayan frontier and in the dry thorn bush of the Chaco of northern Paraguay. Their only contact with civilized man has been in combat. Even the attempts of the Jesuits in the seventeenth and eighteenth centuries to found a mission amongst the Zamucos (an old name given to the Ajoréode – 'men' – as they call themselves) failed on account of the tenacious pride of these tribesmen. Squatting round their campfires in the evening, they still recount how they shook off the invaders' yoke and defeated the white man. The sequel to these early contacts with Christendom was an uninterrupted state of active hostility to penetration by troops, hunters, individual farmers, and recently, to that of companies engaged on a hitherto vain search for oil. It was not until the last twenty years that various missions succeeded in pacifying the greater proportion of this tribe, which does not comprise much more than two thousand souls. In the near future it is envisaged that missionaries will make contact with the remaining 'savages' – as long as the tribesmen are not totally annihilated in the course of their continual fight against civilized peoples.

Racially the Ajoré Indians form a branch of the Mongoloids. They have retained many ancient features such as the Mongolian spot, moderately slanted eyes, heavy cheek bones, straight black hair, a marked supra-orbital ridge and moderately prominent jaws. The colour of their skin is yellowish-brown, which however turns deep brown when exposed to the sun. Dolichocephalic skulls prevail. The Ajoré Indians are of medium height and frequently have athletic constitutions. The limbs and trunk are well proportioned. A marked feature among men is the formation of folds in the scalp, and, as in the case of other Mongoloid races, they have scanty beards. All facial hairs – and body hairs in the case of women – are plucked out singly.

In the course of an ethnomedical expedition in 1969, my wife and I had the opportunity of spending four months among a group of Indians that since 1965 had been cared for by members of the protestant New Tribes Mission from the United States. This tribe had hitherto not been the object of any ethnological studies, so we took the opportunity of recording as much as possible of their original culture before it was rendered unrecognizable by rapid changes brought about during Christianization. The developing mission station is about one hundred kilometres north of the German Mennonite settlements in the centre of the Paraguayan Chaco, from which it obtains all vital supplies. A truck brought us in sweltering heat over roads that are impassable when it rains. Our vehicle was enthusiastically greeted by loud shouts from the Indians as it was generously loaded with sacks of provisions. We regarded the men rather uncomfortably; some had firearms while a larger proportion casually leaned on their spears, the points of which were fashioned from machete blades. Such spears are used for slashing, thrusting or throwing. During the nineteen fifties, the Ajoré Indians had on several occasions at-

The men make clay pipes in which they smoke their home-grown tobacco. Tobacco plays an important part in shamanism; heavy smoking favours hallucinatory experiences but may produce serious signs of poisoning. The shaman inhales the smoke of his pipe until he trembles in a state of trance, during which he comes into contact with various animals that appear to him in the human form of their mythological ancestors. They are believed to help him in healing, rain-making and soothsaying. According to the beliefs of the Ajoréode, the soul of the shaman can enter into actual wild animals and impose his will. For this reason shamans often come under suspicion when someone is killed by a jaguar or bitten by a snake. Under such circumstances it has been known for an unpopular shaman to be slain by angry relatives or a chief.

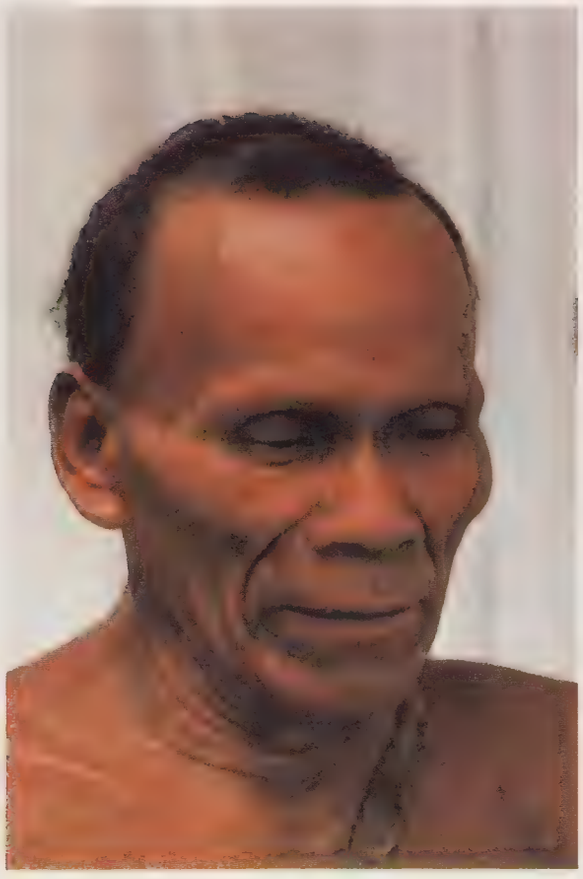
tacked isolated Mennonite farms and taken their toll of the settlers' lives. In 1958, a missionary was speared through the liver for his pains to establish contact with the Indians. And a few months before we arrived, the air had been heavy with evil threats after a dispute over theft in the station's grocery store. But the storm had subsided and we got along fine with the indigenous population, although linguistic understanding was impossible. My wife, who devoted particular attention to the household requirements of the Indians, soon made a number of little friends among the children, and this immediately led to our acquiring the trust and friendship of the adults. The missionaries made us very welcome and placed a small wooden house at our disposal. The dwelling was more or less snake-proof and stood some hundred paces distant from the Indian camp. One of the missionaries, Mrs Joyce Buchegger, generously offered her services as interpreter, which greatly facilitated our task.

The climate of the Chaco is decidedly hard. In the dry season extending from March to August there is invariably an absence of rain over many months. Temperatures can vary greatly from one day to another: from over forty degrees centigrade to a few degrees below zero. In the 'rainy' season, temperatures are more constant and generally lie between thirty and forty degrees centigrade provided the eagerly awaited, scanty rain does not fail. Drought at this time causes the temperature to soar to fifty degrees centigrade; the thorn bush remains forelornly bare; and the north wind blows up swirling clouds of dust that finds its way through the smallest cracks and crevices.

The adaptation of the Indians to this climate is not only manifested biologically but also reflected in their ancient culture. Outside the mission station, their life unfolds with an age-old, seasonal rhythm into which certain religious concepts are integrated. In the dry winter months, small groups of a few related families rove about in their territory and live mostly on a vegetarian diet provided by their womenfolk. Coveted delicacies are obtained by hunting, which is carried out by the men of the tribe. But many of the animals of these parts are taboo; for example, the dangerous jaguar and all members of the cat tribe, the tapir, the stag, and many species of bird. Those who break these taboos and eat such animals are held to run the risk of falling ill or being attacked by a jaguar – their defending and avenging brother. And it is, in fact, relatively frequent that lone Indians are mauled by the beast. Wild pig, ant-bears and turtles are not placed under such strict taboos and are eaten on festive occasions. Water conditions permitting, fish are caught by bows and arrows, baskets, or merely with bare hands. Another task reserved for the male members of the tribe is the search for honey, which frequently involves climbing high and prickly trees. Drinking water constitutes a particular problem. During the long, rainless periods, the shallow water courses, lagoons and water-holes dry up. For a time, requirements are met by rain-water stored in various species of Bromelia and tree hollows, and even simple wells are dug. Otherwise the roots of a certain species of chicory plant *(Jacaratia Hassleriana)*, which have a high water content, are resorted to when necessary.

Owing to the limited amount of food available, the groups are obliged to move on almost every day, several kilometres being covered in the early morning until a favourable spot is discovered. The women carry

a



b

Chief and shaman, about 65 years of age (a).

Young deputy chief, about 30 years of age (b).

most of the household effects and their infants, while the men remain on the alert with their weapons at the ready in case of attack from jaguars or human foes. As long as no danger is present, they relieve the womenfolk of a due portion of their burdens. On such excursions, moreover, paths are used which are kept free by the young men of the tribe, and newly struck if required. Such paths at the same time mark out territories which may attain the size of a country district. No Indian will trespass on the path of another group unless he visits the 'owners' as an ally or intends to attack.

The conditions under which this seasonal tramp is undertaken rule out the possibility of a parent carrying and feeding more than one baby. This occasions the tribal Ajoréode to commit the tragic act of burying undesirable progeny immediately after birth along with the placenta. Little better is the fate of the frail and infirm, especially older people, who are unable to make the trek. Sometimes in accordance with their wishes, sometimes against their will, they are buried alive. This is considered a decidedly beautiful death, as, to the tribesman's way of thinking, the earth harbours neither claws nor teeth, clubs nor spears.

All weapons were originally of wood. In addition to the bow and arrow the Ajoré Indians made extensive use of spears and clubs. Since the war between Bolivia and Paraguay (1932–1936) over possession of the northern Chaco (where oil deposits were presumed to exist) the Indians have been able to find sufficient steel and files to fashion spear and arrow tips. The iron axe has replaced the ground stone axe, and knives of ferrous material are now used instead of tools made from the stone, mussel shells and wood.

When the rains come – about the end of August – the asohna begins her nocturnal song. She is a small bird belonging to the goatsucker family which hatches its eggs on the ground. During the dry season this bird is scarcely ever seen or heard. After the Sun, she is the most important divinity and very much feared. At the first sound of her song, Ajoré Indians congregate in the central villages, where they live together for six months in bands of fifty to a hundred people. On coming together, they perform a ceremony designed to obtain the favours of the bird-god and ensure abundant rainfall. The men then clear a patch of bush and, after the first rain, sow pumpkins, melons, beans, maize and tobacco. But during this initial period the Ajoré Indians still rely on the bush country for food. Small groups accordingly continue to leave the village, or individuals

For making clothes – small fringed aprons for the men, large doubled hip-cloths for the women – these Indians use the fibres of a certain slim species of Bromelia. The green parts are first of all removed by energetic screening, and the fibres produced then hung up in the sun for drying and bleaching.

The dried fibres of Bromelia can be made into thread or rope. Here, a climbing rope is being made that is useful in collecting honey. Passed round the tree trunk and the climber's back, it enables an axe to be used with both hands.

comb the vicinity in daily excursions, threading their way through the prickly plants on each side of the paths. Some of the men take part in lengthy hunting expeditions while the women remain in the village to look after the children. Even at harvest time, the cultivated fields only provide a really adequate communal supply of food for a few days, so the women are almost always busy collecting wild fruits and vegetables – of which there is a far greater abundance and variety at this time of the year than in winter. Summer is the season when most of the visits to friendly Ajoré groups take place and young people are given the opportunity of finding non-related marriage partners. It is also the time for settling old scores with enemy elements in the tribe, as well as for conducting campaigns against neighbouring tribes and white settlers.

The unending wars are to no mean extent due to the sense of values nurtured by the culture of these people: the greatest virtue a man can have is to be fearless; and this can be most readily proved either by fighting men or the larger members of the cat tribe. Whoever kills a man or a jaguar receives the title 'Asuté', chief. During hostilities he leads a subdivision. In attack he is always the first, in retreat always the last. Supreme command is accorded to the chief most renowned for his bravery and accomplishments. At the mission station this position was occupied by a man about sixty-five years of age who also counted as the most capable medicine man. The influence exerted by this man, even in connexion with the acceptance of Christianity, cannot be overestimated, although the tradition of these Indians does not accord such authority purely on account of rank. Such influence depends rather on personal qualities. High chiefs and accomplished medicine men were granted the right to have two or more wives. Moreover, as they could also lay claim to part of any large kill after a hunt, it had always been easier for them to keep large polygamous families.

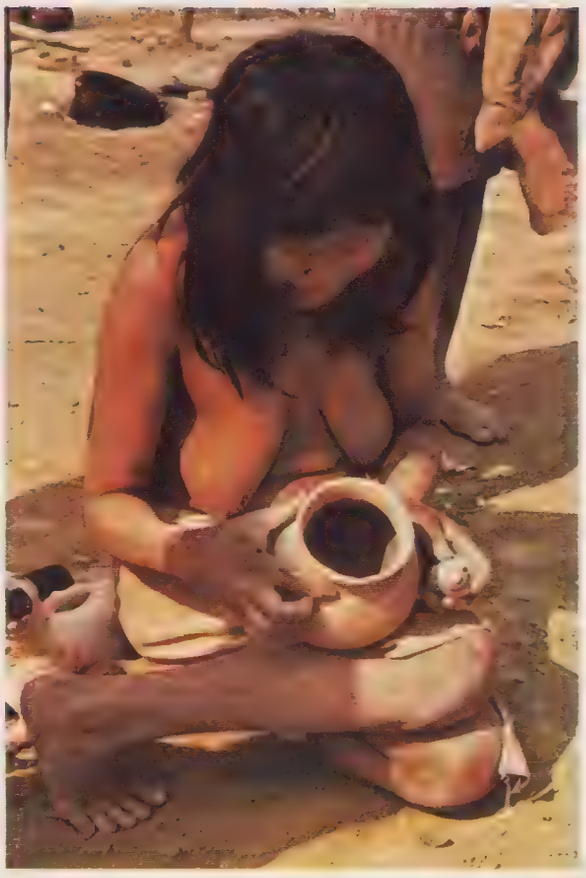
Women eschew politics and busy themselves with manual tasks, food collecting, and looking after children – while in love affairs and the choice of a marriage partner they invariably take the initiative. It is nevertheless evident that the men decide what is to be done and do not hesitate to enforce their will with the aid of a sound thrashing.

These original behaviour patterns were to a large extent still intact during our visit to the mission station. They were completely intact for Indians preferring the old form of life to the new. Such tribesmen spent the greater part of the year in the forests and only turned up occasionally at the mission in order to satisfy their curiosity, visit relatives or barter. Although the missionaries are trying to allow as much as possible of the old culture to continue, Indians closely connected with

With the help of a perforated wooden or wire needle women are here knitting bags with a fine geometrical pattern in a three-colour combination. The thread from Bromelia fibre is either left in its natural white state or stained red with fruit juice or a ferrous mineral dye.

a

Drinking water is a great problem for the Ajoré Indians. Some relief from critical shortages is obtained from plant life: (a) rain-water remains trapped between the leaves of various species of Bromelia for long periods. (b) With the aid of a primitive wooden spatula, this woman scrapes a root of chicory in a home-made wooden vessel. The liquid pressed out of the scrapings is very aromatic and refreshing. One root can supply more than a litre of liquid.



b

Women are making earthen pots for cooking or water carrying. The method employed is to crush a few old fragments of pottery into a powder and mix it with water and fresh clay. The mass is carefully kneaded and formed into long rolls, which are then placed together spirally to form a pot. After laying each ring of the spiral, depressions are evened out between finger and thumb and smoothed with a piece of wood or the shell of a snail. Freshly made pots must dry for several days in the sun before being fired in an open fire. Pots used for cooking have a wide opening at the top while those for water carrying narrow down to a neck. In both cases the bases are conical. This means that the pots are unable to stand on flat ground but this shape gives added strength and the vessels are not so easily broken.

the mission have adopted European ways and thought. A rapid cultural change has thus been initiated, which will most probably spread to Ajoré relatives still living in the forests. Indeed, much of their original, wild spontaneity has already been lost. During our stay, the Indians feared – doubtless without any real justification – an attack from hitherto non-missionized and enemy tribal groups and discussed a preventive sally. This idea was finally abandoned – quite possibly by Christian precepts being brought to bear by some of the influential chiefs. Divorce and beatings are now rarer than before and almost all neonates are allowed to live, which means that families tend to grow

The Ajoré Indian hut can be quickly erected. Brush wood is laid over a few slim tree trunks, reared against one another in a circle and daubed with clay. While on semi-migratory excursions, the Indians only build a hut when it rains. It provides shelter from rain and sun but not from the cold south wind. A fire is kindled to provide light and warmth, and in winter the Indians often sleep between two fires.

larger. A few weeks a year must now suffice in order to satisfy their urge to roam. For the rest, the missionized Indians prefer to remain at the station, where, in exchange for skins traded or work done, food is to be had that is undoubtedly far superior to the bitter fruits of the bushland. European clothes and hairstyles find ready acceptance, food taboos are ignored and Bible texts rank equal with old local myths on the origin of all things – both versions being considered valid. Humility and obedience come into conflict with the old spirit of independence, where it was up to the individual whether he obeyed the chief or followed his own inclination.

By pacification of the Ajoré Indians, the missionaries have undoubtedly saved them from being wiped out by military action. For the tribesmen's extreme xenophobia and warlike ways would have come into sharp conflict with the slow but sure development of their country, making their extermination merely a matter of time. It now remains to be seen whether the missionaries are also successful in preserving the Ajoréode from sharing the fate of neighbouring tribes – in sinking to the lowest possible proletarian status of the nation and leading an existence far unworthier than the one they enjoyed before their contact with civilization.

Indians at the mission station learn to build their own accommodation from forest materials. Unlike their traditional tribal huts, these dwellings are capable of withstanding the winds and rains of these occasionally inhospitable regions.

Gastric Chromography

Hugo P. Tomatis,
Francisco Germano
and Ricardo Hans

The broadening of our knowledge on the physiological and physiopathological aspects of gastric secretion in recent years has resulted in many surgeons having a wide choice of techniques at their disposal for treating duodenal ulcers.

Today, such methods as the two-thirds or three-quarters gastrectomy (Billroth I or II), vagotomy with drainage (pyloroplastic or gastroenteroanastomosis) or antrectomy are no longer considered as 'competing' with one another; the form of surgery eventually selected is based on results obtained in quantitative secretion tests (basal secretion and response to maximum stimulation), X-ray findings, and clinical history.

The transilluminator employed, with cold-light source. A smoked-glass panel on the upper side of the metal housing ensures a uniform degree of lighting. (The instrument is manufactured by Laboratorios Electrónicos Gottlieb, Córdoba, Argentina.)

Canine stomach, stained as described in the text, resected and opened along the greater curvature. The difference in colour between the antrum and the corpus is very marked. The acid-secreting cells of the corpus had been stimulated and the pH value of its walls considerably reduced. The Congo red introduced has consequently been fixed and given the corpus walls an intense colouring, whereas the antrum, which has no acid-producing cells, has remained colourless.

While almost all the above methods can easily be carried out and used successfully by every experienced surgeon, a 'blind' antrectomy nevertheless invariably leaves the surgeon room for postoperative doubt regarding accuracy of the resection. The Japanese surgeons Oi et al. (1959) found there were appreciable individual variations in the position of the boundary between the antrum and the corpus. The boundary, which is dependent on the shape of the stomach, was shown by these authors to lie usually at distances of 7.5 cm from the pylorus on the lesser curvature and 6.5 cm on the greater curvature. But in extreme cases the antrum can extend as far as 16 cm from the pylorus. The breadth of the transitional zone between the pyloric antrum and the corpus was in some instances 0.2 to 2 cm, but generally it did not exceed 0.5 cm. The American authors, Ruding and Hirdes also worked on this problem in 1963. They recommended the resection include four fifths of the lesser curvature so as to ensure radical removal of the antrum, while the line of resection on the greater curvature should run much closer to the pylorus.

Many methods have been described for determining the corpus-antrum boundaries in individual cases. They all hinge on the acid-secreting function of the parietal cells in the mucosa of the corpus and the total absence of such secretory activity in the pyloric antrum.

Using a glass electrode, Capper demonstrated in 1963 that it was possible to detect, intraoperatively, pH differences on the gastric mucosa.

A year later Bengström and Broome succeeded in determining the boundary between the antrum and the corpus by means of a colour indicator (after intragastric spraying with Congo-red dye via an esophageal route); they demonstrated the accuracy of this chromographic method by gastrotomy and direct visual examination of the mucosa.

In 1966 Moe et al. described a combined application of chromography and transillumination. Hendestedt et al. also worked on this method and introduced a few modifications.

Two years later Ottenjann et al. described their own technique for delimiting the antrum-corpus boundary: after chromography as per Bengström and Broome they conducted a gastroscopic examination of the course followed by the boundary. By means of a needle introduced through the gastroscope, they marked this boundary by inject-

Posteriorly transilluminated stomach after application of colour indicator as seen by the operator. Contrasted with the dark corpus, the antrum appears clear and translucent.

ing Indian ink into the stomach wall. The authors claim that this 'gastric tattoo' can be seen on the serosa and provides the surgeon with a useful guide.

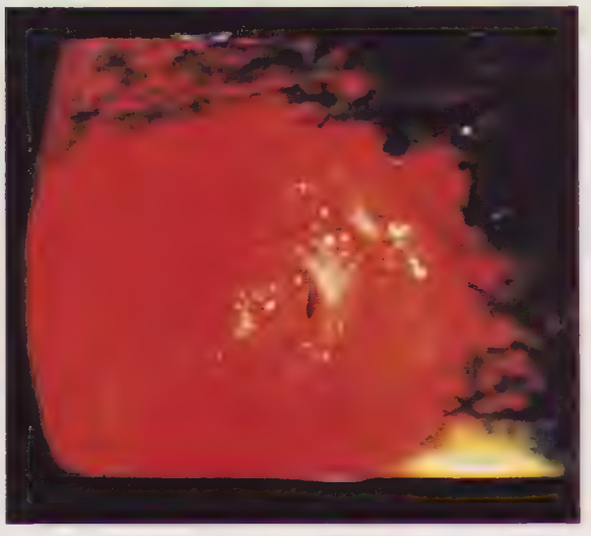
Our own experimental technique

Our method was developed by studies carried out on dogs that had fasted from twenty-four to forty-eight hours. This ensured that their stomachs were completely empty. They were put under general anesthesia with morphine hydrochloride. By means of a nasal catheter gastric lavage was performed using a five per cent solution of sodium bicarbonate in order to neutralize all hydrochloric acid of the gastric juice. Thirty cubic centimetres of Congo-red dye was then introduced through the same tube, followed by 2 mg of seven per cent betazole per kilogram bodyweight. Half an hour later the operation was commenced. After the stomach had been exposed we opened the greater omentum and were then able to place the transilluminator in position.

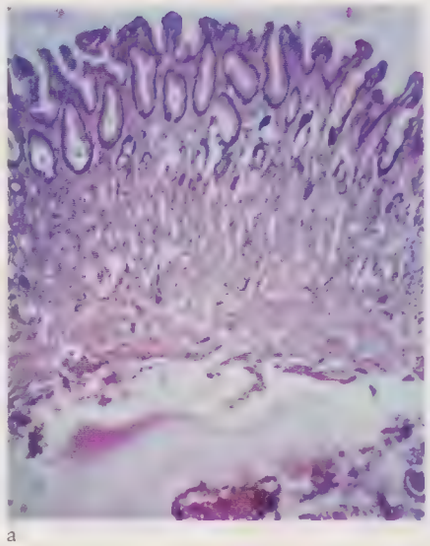
As soon as the apparatus was functioning it was possible to see the bright, translucent image of the antrum which was clearly distinguishable from the dark, opaque corpus.

This difference arises by virtue of the fact that when stimulated the cells of the corpus wall secrete hydrochloric acid and lower the pH value below 3 – ensuring that the Congo-red dye takes on an intensive colouring and becomes fixed in that area. The walls of the pyloric antrum have no acid-producing cells: their pH value is higher and Congo red neither takes on any colour nor is fixed. For this reason the antrum has a translucent appearance under transillumination. The antrum-corpus boundary is marked with sutures which are used as a guide for the resection. Histological examination of samples taken from both sides of the boundary established have revealed marked differences in mucosal structure.

The aim of our experimental work has been to standardize the individual steps taken in such surgery and objectify the findings made in the course of these studies.



Gastroscopic photograph clearly showing the dark staining of the corpus and the unchanged appearance of the antrum after the instillation of Congo red. At this stage OTTENJANN marks the boundary by 'tattooing' the stomach wall with Indian ink. Photograph by Dr. R. OTTENJANN, Senior Lecturer at the University Clinic, Erlangen, Nuremberg.



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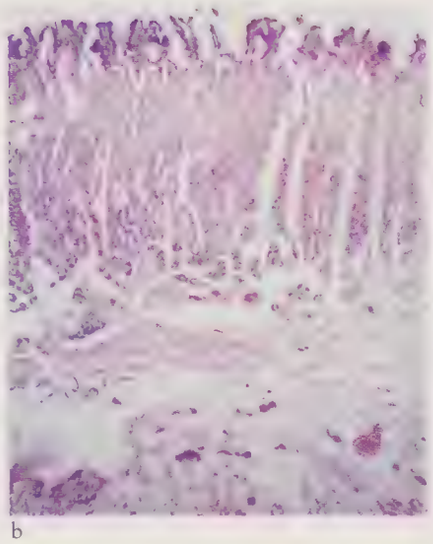

b

Histological samples of mucosa from the oral and aboral edges of the sectioned wall of the stomach immediately after resection. This histological examination demonstrates perfect agreement between chromographic and morphological findings. (a) Sample taken from the oral edge of the resection, i.e. from the corpus. (b) Sample taken from the aboral edge of the resection, i.e. from the antrum. Staining: hematoxylin-eosin (×35).

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59 015

Edible Figurines

Gabrielle Wittkop-Ménardeau

In describing the last rites accorded to Patroclus by Achilles, Homer mentioned how twelve Trojan prisoners were sacrificed in order to provide the dead hero with a retinue for the other world. Such funerary rites were practised in almost all civilizations and in Lithuania actually persisted up to the end of the fourteenth century. The deceased left for the great beyond with part of his possessions, accompanied by pets, servants, even best friends. But sooner or later the offering of sacrificial substitutes was inevitable, if only to do away with the economic and domestic chaos that must have arisen from such habitual funerary hecatombs. So sometimes a lock of hair – *pars pro toto* – became to be considered sufficient, sometimes a bracelet. Signifying mourning, renouncement and penitence, these burial objects were in turn replaced by substitutes, among which were articles modelled in bakers' dough. The Egyptians, Greeks and Romans used dough made from wheaten flour for baking such ritual figurines.

The baking of bread had for long been subject to extremely strict regulations, standards, taboos and even complicated ceremonial procedures. As a consequence, this ductile, readily available material was invested by the imagination with highly magical qualities, and the ineluctable mystique surrounding the bread figurine made it suitable for depicting almost any creature or object. It is therefore hardly surprising that the human form itself would eventually be called on to assume a major role in such an expressive medium. Hardly any emblem had been omitted: the figurines baked ranged from representations of the solar disc, symbol of the creative force, to the toad, sign of everlasting life. Both uncompromisingly human forms and demons with human attributes ranked high in the edible idiom: infinitely higher in sacrifice than other depictions. As most of the sacrifices were of a propitiative nature, it is obvious that those accompanying fertility rites were largely intended to appease the spirits of the departed or those which might oppose fecundity. That period of the year when winter neared its end and spring began was not only dedicated to fertility rites but also to purifying fasts, to ancestors or to dreaded divinities susceptible of exerting evil influences on seed. These aspects are reflected in the great feast in honour of Huitzilopochtli, an important event of ancient Mexico celebrated in the fifteenth month of the solar year; the priestesses moulded a huge figure of their god from vegetable seed and infants' blood. After the customary holocausts, sometimes involving human sacrifices, the high priest broke the effigy with an arrow and distributed the pieces to those present. As in numerous cults of spring vegetation (e.g. the passion of Osiris) the effigy of the god was identified

Crude, lacking in subtlety, this bread baby appears rather to have been moulded from clay than dough. It is obvious that the baker has not made the slightest attempt at artistry: its purpose is evidently served if the form is recognized, and above all, its strong magical significance remains anchored in the consciousness of those eating it. According to Max Höfler the bread babies of Transylvania are known as 'little house fathers' which correspond to the Russian *domovoi* or household genius. This particularly seems to indicate that the 'little house father' is identified with the penates or Roman gods of the household: Athenaeus mentioned the wide use of the term 'little father' by the Greeks in certain invocations and wrote that when they appealed to the dead for a love spell they ate bread called ἀττάραγοι. In spite of the edict issued by the council of Liptin in A.D. 743 prohibiting the moulding of 'idols from consecrated flour', Christianity did not succeed in banning the 'little house father' which had somehow become identified in folk art with the Infant Jesus. Original photograph kindly supplied by the Austrian Bakers' Guild *(Bundesinnung der Bäcker)*, Vienna.

The antiquity of this bread figurine from northern Austria is revealed in a truly striking manner. It may have been 12 to 20 cm in height. The features are replaced by a spiral and in place of the pastry ribbons usually decorating the swaddling clothes are diamond-shaped grooves, from time immemorial the symbols of feminine fertility. Original photograph kindly supplied by the Austrian Bakers' Guild *(Bundesinnung der Bäcker)*, Vienna.

In the second week of March it was the custom in Brunswick, Germany, to bake rings of linked infant figures; in the Lübeck region it was a tradition to present newly engaged girls with a butter baby. In the Tyrol there is a type of pastry exclusively reserved for the bride which is decorated with five or six edible dolls. These babies of butter, cake or pastry are typical fertility symbols and all possess the archaic form of babes in swaddling clothes lying on a cushion. The figures of marzipan or spiced bread are sometimes provided with a paper base. In parts of Yorkshire, England, it is a spring custom to bake a large doll of bread and dress it up in real baby clothes. From the collection of Max Breitschmid, Basle. Photograph by Peter Heman, Basle.

with the offering before being distributed among the faithful as bread.

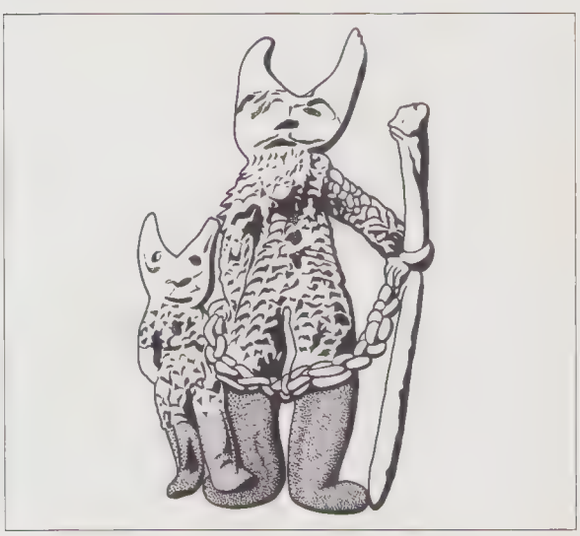
In all fertility rites, the notion of plant fertility is inseparably bound up with that of animal reproduction. The awareness of this bond, frequent among primitive peoples, rare among populations of more sophisticated cultures, generally finds parallel expression in bread manufacture and reproduction (an association even encountered in psychoanalysis). As man almost invariably attempted to further reproduction of his species with the aid of imitative magic, bread figures made their appearance in the form of men, women and particularly babies, not only in festivities connected with crops but also in marriage feasts.

Yet even in winter, grotesque figurines appeared on the scene such as *Krampus*, which bakers of German-speaking countries still sell on St. Nicholas Day. Legend has it that the Bishop of Myra captured a devil and kept him as a famulus – a story casting a somewhat dubious light on the perspicacity of the saint; far from being a good servant, *Krampus* fully retained his character as 'plant demon'. In certain districts of Austria he is known as *Hidlbua,* in others *Niglo*. The latter suggests confusion with Nicholas – borne out in some measure by the horns of *Krampus* being mistaken for the tip of the saint's mitre.

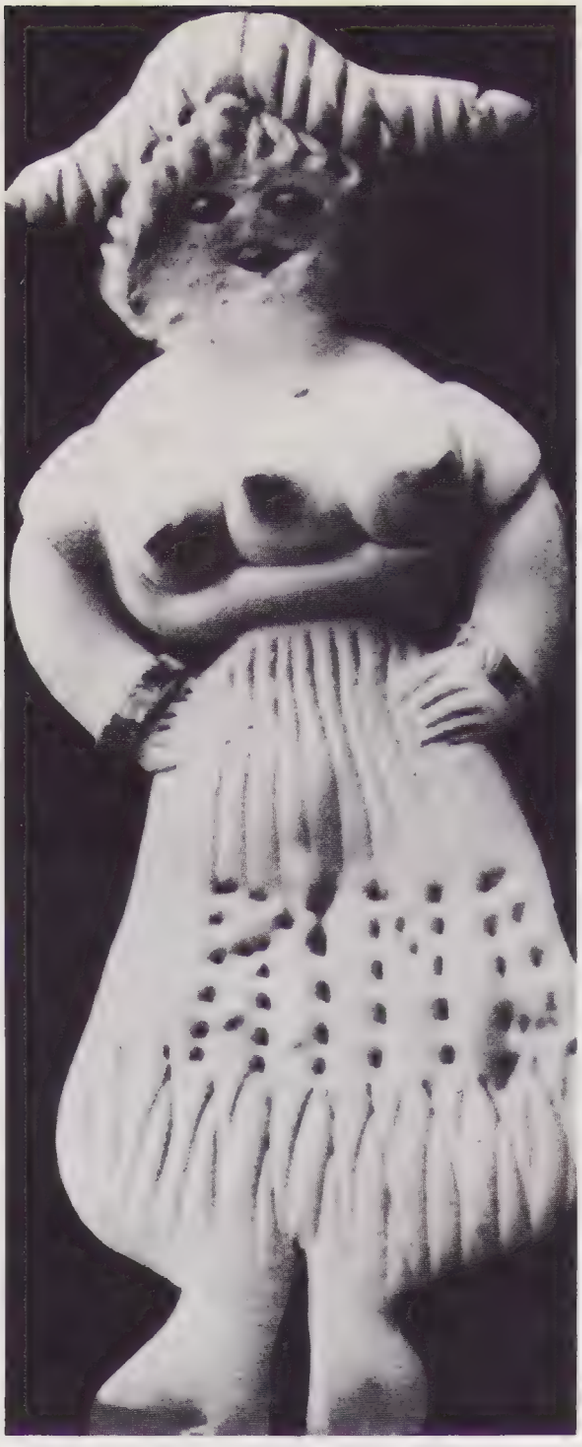
This figurine of an earth-bound devil looks as though he had just sprung from the *cortège* of the great god Pan. But here, his phallic air has been tempered to one of bucolic serenity and the attribute of generative strength has simply become one of animal agility. Merry and innocent in its antiquity, the carefree face of this devil is not exactly lacking in malice. For in order to share the fruits of the earth with men, he would need his portion of cunning. From the collection of Max Breitschmid, Basle. Photograph by Peter Heman, Basle.

Always ready to laugh, and with the dark gaze of his raisin eyes focused on the observer, *Krampus* sometimes appears accompanied by a small double. This is to lend force to the notion of his fertility and continual rebirth. The baker works on the surface of the dough with a pair of scissors or – if the figure is small – with the point of a needle so as to give the impression of furs. The poppy seeds covering the legs are intended to depict leather boots. This excellent figurine is some 50 cm high and stems from Linz in Austria. It is presumably connected with the 'wild man' of Germanic folk law who participates in processions about the time of the winter solstice and represents a plant demon. Original photograph kindly supplied by the Austrian Bakers' Guild *(Bundesinnung der Bäcker)*, Vienna.

A fine stylized figure formed by two pastry serpents stemming from Graz in Austria. The eyes of this *Hidlbua,* as well as its mouth and shoe tassles, are made of raisins. The form is unique in its stratification and depth of superimposed symbols: here the figure of the plant demon corresponds to that symbolizing the marriage of serpents, a hermetic symbol, that in many races was closely related with a cult of the dead and certain rites accompanying sowing. Original photograph kindly supplied by the Austrian Bakers' Guild *(Bundesinnung der Bäcker)*, Vienna.



This ingenuous figure of a siren appears here in medieval form, the customary wings and bird's feet of classical times being absent. Cake from Frascati.



What has happened to the gods of antiquity now that sculptors no longer seem capable of hewing them out of their marble medium? Have they, in borrowed guise, taken refuge with some Italian baker? Diana genitrix, revered in Ephesus, seems to be hidden behind this harlequin figure of the *Commedia dell'arte*. The half-moon has been stylized into a two-pointed hat while the breasts, which once entirely covered the bust of the goddess, have been reduced to three. Cake from Frascati.

St. Nicholas is sometimes even taken to be the wife of *Krampus* (*Krampusweibl* in south German idiom) on account of the similarities existing between sacerdotal soutane and female frock. It is clear that the terminology is fluid, while the symbols themselves intertwine and overlap.

During the Middle Ages the baking of pastry figurines spread throughout Europe. But while such cakes in doll form were openly on sale in the streets of Paris, a thirteenth-century Norwegian edict prohibited bakery products depicting human features, severe penalties being promised for non-observance.

Typical of imitative magic was the gingerbread man. He appears in many old English folk tales, the most famous of which is that of a couple who were troubled by their inability to have children and baked a gingerbread man in the oven. At the fair held near the cathedral of Frankfort on the Main shortly before Christmas, it is not only still possible to buy (invariably disappointing) figures of spiced biscuit but also rather remarkable *Zwetschgenmännchen*. These are made up of prunes skewered on a wire skeleton with a nut as a head. . . .

But the depiction of the human form in edible substances is by no means limited to babies, demons and manikins: couples appear to be a very popular theme too. In Antwerp, Zurich and Swabia it was customary

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This figure from the 18th century does not seem to have any direct bearing on the ancient myths – unless it could be argued that every fashionable woman were something of a Venus. This is undoubtedly not intended to be a personification of any figure but rather a depiction having a purely social symbolism – that of a young woman, beautiful and rich, becoming as much an accepted part of the hierarchy as 'the hunter', 'the gardner' and 'the confectioner'. The expression of the cascading folds of lace leaves us at a loss which quality to admire – simplicity or sophistication. From the collection of Max Breitschmid, Basle. Photograph by Peter Heman, Basle.

at Carnival for young people to exchange presents consisting of plum cake in male and female forms – a ceremony invariably accompanied by rather robust humour. In Schmerikon, in the Swiss Canton of St. Gallen, girls presented their admirers with a *Küchlifrau* of spiced cake. Couples depicted in similar media appeared on the scene at a relatively later stage and became a traditional confectionery figure at wedding feasts. Intended to represent the bridal pair, this figure really symbolizes the couple as an entity, as an abstract element of the perpetuity of the species. It was a notion extending beyond the personal sphere, beyond even the biological male and female concept, to the cos-

In the 18th century 'pastorals' enjoyed a revival. They expressed the nostalgia of city people already burdened by urban restrictions and satiated with life's artificiality; in this mode of expression they hoped to find salvation in what was an even more artificial 'simple life' in the bosom of 'innocent nature'. It was an escapist disguise. Even Adam and Eve were not excluded from this fashion, which reached its climax in the *Hameau* of Marie-Antoinette. From the collection of Max Breitschmid, Basle. Photograph by Peter Heman, Basle.

mic concept of heaven and earth, sun and moon. The couple figures of the seventeenth century were sometimes modelled with such ornate extravagance in *bas-relief* marzipan that the City Fathers of Nuremberg proclaimed a sumptuary edict imposing a fine of five florins on those failing to observe greater austerity. Most of the edible figures had by this time lost their magical meaning. Like the coloured confectionery used by Jacopo Sansovino to garnish the tables of show-conscious Venetians a century before, they were just another of the many and diverse facets of baroque fantasy.

Yoked to the seasonal rhythm of rural cultures, the old figures in bread and pastry

These two musicians from the 18th century were probably intended to accompany figures in a group of spiced cake forms, presumably depicting pairs of dancers. These musicians are most frequently encountered in all forms of wedding pastry and even in models of the same material representing the bride and bridegroom. In his *Nut Cracker and Mouse King,* E.T.A.Hoffmann described figures which children played with before eating, and which were known as *Thorner Katharinchen:* '... a few fine little brown men and women with golden faces, hands and legs. They all came from Thorn, smelling sweet and pleasant....' From the collection of Max Breitschmid, Basle. Photograph by Peter Heman, Basle.

The Hussar was a quasi mythical entity in the world of the child and in ethnic environment. Modelled in lead and tin, carved in wood, the figure was of course also baked in spiced bread. Stemming directly from the type of figures hawked from door to door, this Hussar is given a noble air and has a pleasant eye-catching elegance imparted by the rhythm of the curves on the right side. From the collection of Max Breitschmid, Basle. Photograph by Peter Heman, Basle.

A rural world of charm and harmony frames the Adam and Eve of this Hungarian baking mould. Vertical and horizontal components give delicate balance to the composition, which constitutes the artist's basic concept of creation. The stability and the continuity of rural life is unaccompanied by any striking artistic innovations: the ageless, fresh quality of such work makes the dating of it frequently difficult. Iparmüveszeti Museum, Budapest.

This waffle iron pattern made by a village smith depicting a fully clothed, grotesque Adam and Eve doubtlessly reflects some of its author's own displeasure at the plucking of the apple and its tragic sequelae: the endless chores of holding together house and home and the unremitting struggle to ensure procreation of the species. The Minden Museum of History, Geography and Ethnology, Minden, Westphalia.

could hardly hope to thrive in an increasingly urbanized eighteenth century: new facts ousted old phantoms, while under the influence of culinary refinements, *Krampus, Grittibenz* et alia became purely brioches, puff-pastry, and there was an ever-growing tendency to replace figures of confectionery by those of china. But children were reluctant to forego the delights of edible figures so that in the eighteenth and nineteenth centuries extensive use was made of a highly plastic substance made from tragacanth, sugar, flour and vegetable colouring. Figures made of such ingredients found their way into many dolls' houses and were eventually consumed by their child owners.

The sculptor Thorwaldsen is sometimes said to have discovered his vocation of choice while modelling a figure in pastry. Or did this story arise merely because *all* his works have the appearance of being sculptured in edible material? It is hard to know where truth ends and bias begins. But such culinary influence cannot be doubted in the case of Canova, an artist, whose Psyche and Venus creations so often look like melting confectionery and tell of his early apprenticeship to the trade.

Commercialized and mass-produced, the edible figure in human form no longer basks in the ancient light of magical attributes and enjoys but an etiolated existence. A wan sign of its survival is the rather banal chocolate doll. Only a small band of hardy veterans such as *Krampus* and the manikin of prunes still gallantly hold on in a world far too busy with space trips and nuclear discoveries to pay them much attention.

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The world of the neurotic
The neurotic lives in a vicious spiral of mutually interacting and intensifying conflicts and reactions, which can only be broken by a time-consuming process of deconditioning coupled with support and insight. While the foundation for such treatment of neurotic states remains psychotherapy in its various forms, the dream of many psychiatrists from Freud onwards, has always been to possess drugs which could exert a selective influence on psychic and emotional components instinctive drives and even the structure of the personality.
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prolonged	lasting about 8 hours[3];
natural	the sleeper can be readily awakened, regardless of the dose he has taken;
restful	he wakes feeling refreshed[2].

N.H.S. GENERAL BENEFIT

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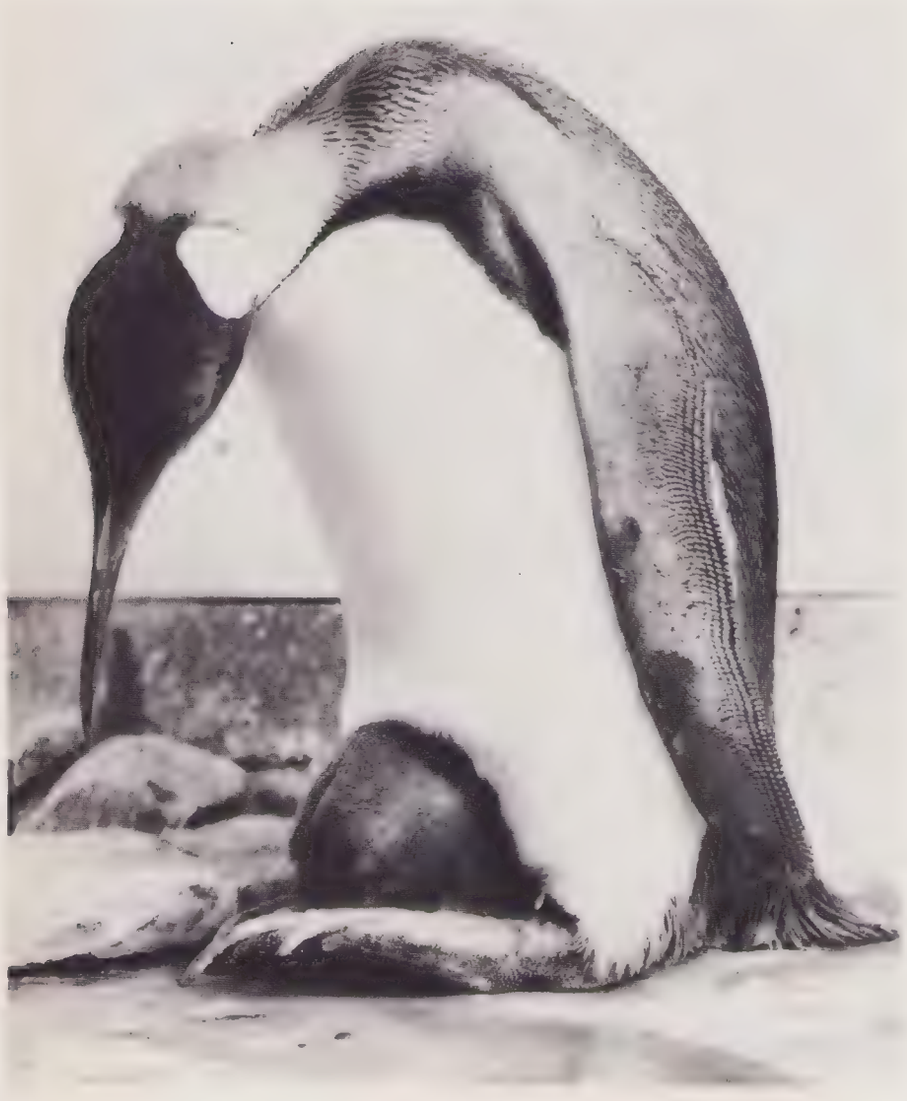
On His Own Two Feet

The rearing of the young king penguin

Ernst M. Lang

Penguins in zoological gardens tend to steal the show be their erect posture, somewhat human movements and a tuxedo-clad appearance. The latter is in reality however a most efficient camouflage: the silvery underside of a swimming penguin viewed from below can scarcely be picked out from the surface, while its dark back seen from above blends with sombre Antarctic waters. The penguin's most dangerous foe is the leopard seal, which hunts the birds when they dive. This large, spotted animal skins penguins with a few movements of its sharp teeth and swallows their denuded bodies in one piece. As penguins have virtually no natural enemies on land, they are usually very tame.



Both the egg and a newly hatched young bird are covered and kept warm by the feathered abdominal fold of the king penguin. This fold corresponds to the brood patch of the song bird, where there are extensive capillary circulation and naked patches, and by contact with which the egg or young are kept warm. The abdominal fold is often raised by the incubating penguin when it wants to look at the egg or show it to its mate. The king penguins of the Basle colony are individually marked by a plastic band attached to the wing giving access to such data as the bird's age and mating conditions.

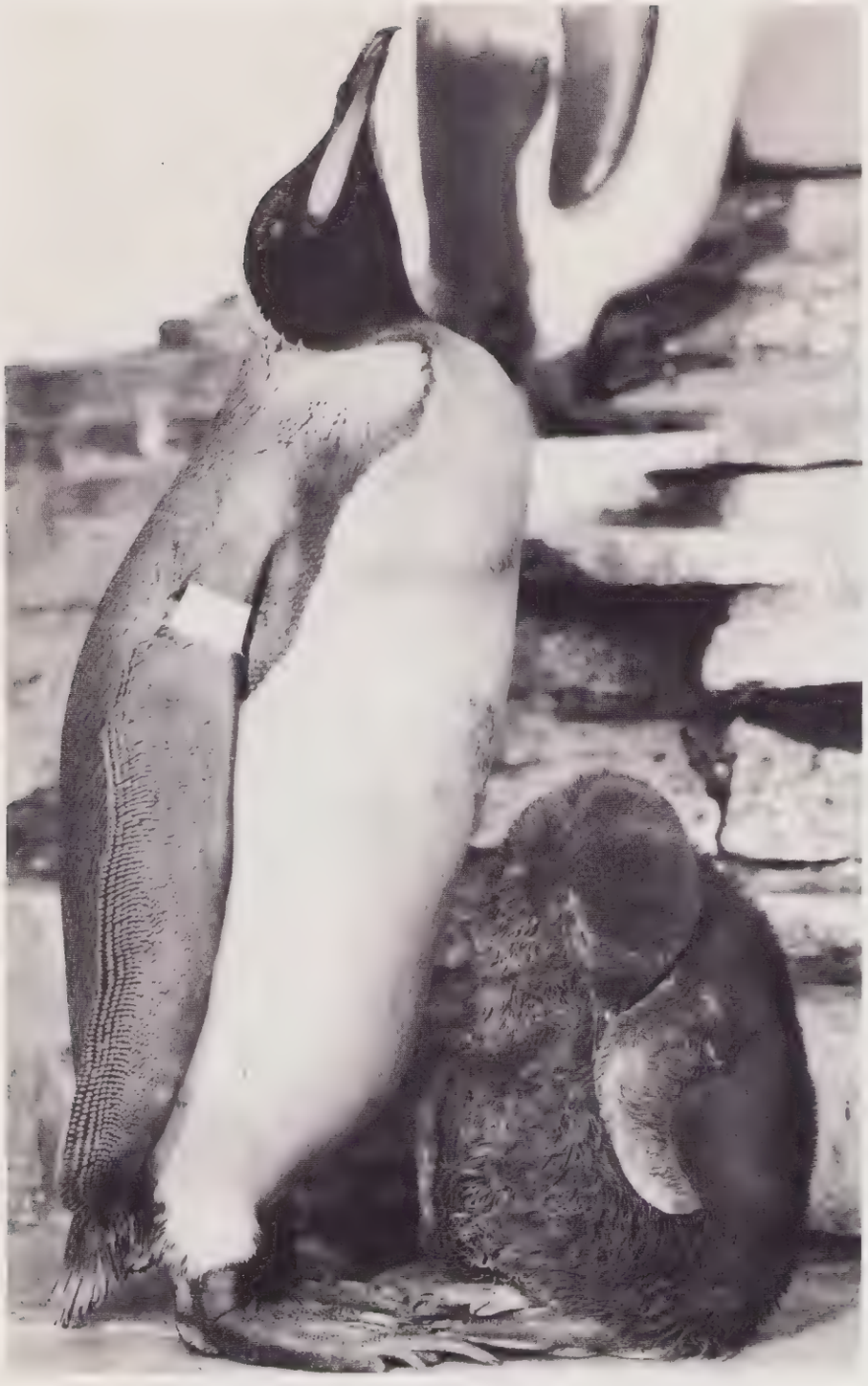
Three to four weeks after being hatched the young penguin is covered with a downy 'duffle coat' and stands more or less on his own two feet. At this early stage he already sticks his beak under his wing when sleeping in order to breathe in pre-warmed air. When he is cold he raises his feet from the floor and thus avoids loss of heat on the cold cement flooring. Recently we have had the cement slabs covered with insulation material, so that the penguins can live in a cooled room without having to give up heat to the flooring.

Penguins occur only in the southern hemisphere, where, however, seventeen species are found, from the Antarctic up to the Equator. The smaller species live on the Galápagos Islands and around the tip of South Africa. The smallest penguin of all, however, is found along the coasts of Australia, while the largest inhabit Adelie Land around the South Pole on the edge of the Antarctic continent. Since the French Antarctic expedition conducted studies on the emperor penguin over several breeding cycles, we know quite a lot about the biological aspects of the manner in which this largest of the penguins incubates its eggs. The bird builds no nest, but rolls the egg onto the top of its feet and covers it with a feathered fold of abdominal skin. The actual incubating occurs while the animals are standing together in large colonies during the Antarctic winter, often at —40°C! After hatching, the young are also kept warm in this manner and fed from their parents' stomachs.

The colony of king penguins in the Basle Zoo also incubate without nests. Unlike the emperor penguins, however, they make their appearance on the breeding grounds when the days begin to lengthen, i.e. in the Antarctic spring. The air is often filled with the mating calls of thousands of birds which later pair off for copulation, egg laying and incubating. Inhabitants of the subantarctic and temperate cold zones, king penguins gather into enormous rookeries in the Falkland Islands, South Georgia, Kerguelen and Macquarie, as well as on other islands in these latitudes.

In 1969 the breeding behaviour and growth of king penguins was observed in close proximity at the Basle Zoo. Before the breeding season commences, the penguins moult. They usually remain standing in the same place and lose their entire coat of feathers. But new feathers appear immediately after the old ones fall.

It is only after they have moulted that the pairs are ready for breeding. Before the laying of the egg, both partners appear frequently together and emit trumpeting tones from outstretched necks. When the female lays the



egg on the bare ground, she immediately turns round and rolls it with her beak onto her feet. The egg is then enveloped in a fold of abdominal skin resembling a pouch, which hides it from view. The incubating penguins can, however, be immediately recognized by their posture; they appear smaller, hunched on their heels, while the lower end of the abdomen has an outward sweep. In view of the low ground temperature in subantarctic regions, this manner of incubating is very suitable. The bird is in fact capable of moving small distances with the egg on its feet. Now and again the partners take over from each other in their incubating chores. When one partner is ready to relieve the other, it points to the egg with its beak. The bird with the egg then raises its abdominal fold, and the other carefully rolls it onto its feet with its beak, covering it in the manner already described. Both parents incubate the egg for irregular periods. As under such conditions it is difficult to differentiate between male and female adult birds, we are unable to say which partner spends the longer time incubating the egg.

After an incubation period of 53 to 54 days the young bird is hatched, and it is not long before he announces himself in shrill tones. He makes his debut into the world with a coat of grey down but continues to be kept warm under the abdominal fold by standing on the parent's feet. Fed by the adult bird from the stomach with predigested food, the offspring remains in the pouch as long as there is still enough room. Later, he is content merely to place his head between the feet of the adult bird in order to be huddled.

About three weeks after being hatched he stands more on his own two feet and begins to walk around. He is covered by a brown 'duffle coat', which soon consists of rather long down and provides excellent insulation. When he begs he taps his beak against that of the adult bird and as soon as the latter is ready to feed him, sticks his beak deep into the mother's gullet and receives regurgitated mash. He must often swallow thick lumps of food.

Growth is rather rapid. A young bird hatched here in the zoological garden weighed 2.5 kg in 28 days, 8.6 kg in two months, 12.1 kg in three months and 14.4 kg at the end of five months. At the age of eight months he attained a weight of 17.3 kg! This made him 4 kg heavier than his parents. For the approaching moulting period, during which the young bird is no longer fed by the parents, he needs ample fat reserves to tide him over the 'growing pains' of independence. At eight months of age the young bird slowly sheds the brown coat of down. When moulting is finished the young penguin stands there as if he had just stepped out of a bandbox and can scarcely be distinguished from his parents. It

The young penguin always returns to his parent to sleep or when he requires feeding.

On cool days, and in summer only in the early morning, the penguins are allowed to leave their 'air-conditioned house' in order to swim in the clean water of the moat enclosing the reindeer. They are thus exposed to tolerable amounts of the usual germs of our environment, and over the years they evidently develop a resistance – particularly when kept on a balanced diet. Individual king penguins have lived in the Basle Zoological Garden for twelve years or more – a figure that, moreover, still does not correspond to their normal life expectancy.

is then that he goes into the water for the first time to swim and dive.

Difficulties are inevitably entailed in keeping the larger varieties of penguins in captivity. In their natural Antarctic habitat the birds live in an almost germ-free environment. Exposure to unaccustomed germs begins during their transportation to zoos, and the long journey generally causes a deterioration in their condition. On arrival, many penguins suffer from serious infections, particularly aspergillosis, against which they evidently have no resistance. This disease, from which many soon die, is caused by a genus of ascomycetous fungi which spreads over and even penetrates the tissue in the air sacks.

The young king penguin slowly sheds his brown coat of down at the age of about 8 months. After the moulting period it is difficult to distinguish him from the other adult birds. The latter moult before brooding, during which time they remain standing for about two to three weeks on the same spot and rapidly lose thousands of small feathers which tend to accumulate around them in rather attractive circles. Their new plumage forms into a closely interlocked, hard feathery armour which, owing to its capacity to retain air, affords the bird a high degree of buoyancy. On diving, some air is always pressed out from between feathers round the neck, so that when the king penguin swims under water he leaves a trail of air bubbles in his wake.

But when penguins are kept in a closed installation with filtered, refrigerated air and given a nutritious diet, they may live for a long time in a zoological garden and even have young.

In the natural state penguins not only eat fish but also crabs and small squid. In the zoological garden they are fed mostly on herrings and whiting. As most of the vitamins in the fish are evidently destroyed during their lengthy transport and storage, the deficiency must be made up by diet supplements if the birds are to remain healthy. Fish fodder in the Basle Zoo is therefore enriched by vitamins, particularly A, D and E. The following observations demonstrated that under certain conditions king penguins require a high amount of common salt: several adult birds of the Basle colony that had reared young became seriously ill. They were unable to stand up and refused food. One of them died and there were no conclusive autopsy findings. The reason was found to be that in feeding their young with predigested food they had also lost a considerable amount of gastric juice, which is known to contain hydrochloric acid. It follows that if their diet contains inadequate common salt, a rapid depletion ensues producing serious symptoms and possibly culminating in death. On being given salt in gelatine capsules, however, the condition of the sick birds rapidly improved. Since this finding, penguins in the Basle Zoo receive about 2 g of sea salt daily.

Keeping penguins without a refrigeration unit should really be considered zoological 'malpractice'. One of the physical characteristics of these birds is their great capacity to retain body heat. In their natural habitat, superfluous heat does not exist, and once here they fall into a fatal condition should it be necessary to give off body heat. Their feathery covering and the underlying fat are an extremely efficient insulation from which heat cannot escape. The only naked patches occur on the feet and are very small, and little is known about their function as heat exchange organs. Apart from this there is only panting, which is inadequate under our summer conditions to conduct away superfluous heat. A heat build-up may cause acute damage to penguins, but the majority of them first lose their resistance and later die as a consequence of fungus disease. Penguins at the Basle Zoological Garden live in a well-insulated, constantly cooled house where the temper-

ature never rises above 12°C. In addition, two strong ultraviolet lamps are switched on day and night in order to reduce the germ content of the air. Only on cold days or early mornings are the penguins allowed to swim in the nearby pond, where their splendid leaps out of the water could cause them to be mistaken for dolphins.

Every penguin here eats out of the keeper's hand. In this way it is possible to keep a check on whether each bird is properly feeding. As soon as a bird refuses food he is immediately placed under observation. The penguins thus get to know their keepers very well, which can sometimes be a disadvantage as they might refuse food from a new keeper.

The oldest king penguin at present in the Basle Zoo arrived on June 13, 1957, direct from the Antarctic. The second oldest was hatched on July 26, 1959. Perhaps one day we shall reach the stage where these birds attain a normal age of about twenty years even in captivity.

When moulting has terminated it is hardly possible to distinguish the young penguin from adult birds.

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(Lal, S.: Paper, The Synergy of Trimethoprim and Sulphonamides, Royal College of Physicians, London, 9.5.1969.)

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